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Original Communications

SYSTOLIC GALLOP RHYTHM

STUDIES ON ITS CHARACTERISTICS AND MECHANISM

CHARLES C. WOLFERTH, M.D., AND ALEXANDER MARGOLIES, M.D.
PHILADELPHIA, PA.

A SURVEY of the literature dealing with systolic gallop rhythm reveals considerable difference of opinion. Some writers think it occurs but rarely. Others believe it to be frequent. It has been variously described as heard best at the apex, the base, and the mid-portion of the precordium. Some have found it in severely ill patients only; others believe that it may be present under a great variety of circumstances, and regard it as having no particular clinical significance. The chief reason for the apparent difference of opinion is that various authors have included different sounds or groupings of sounds under this designation.

Cuffer and Barbillon[1] are usually given the credit for being the first to describe systolic gallop rhythm. The term actually used in their papers was "mesosystolic gallop." They describe the extra sound as clear, short, and superficial, heard best in the middle region of the heart, and not influenced by respiration or posture, although it may be present on one examination and not on another. They emphasize the fact that the additional sound is separated from the first sound by a very short interval and sometimes seems to merge into it, suggesting a double systole. The so-called mesosystolic gallop rhythm was observed in four cases of typhoid fever and two of tuberculosis.

We have studied Cuffer and Barbillon's papers in an attempt to identify what they were describing. The accounts of the additional sound found in the case protocols reveal considerable differences from case to case, so that certain points of similarity to each of the following may be noted: (1) reduplication of the first heart sound, (2) presystolic gallop rhythm, (3) the sound later described by Gallavardin[2]

From the Edward B. Robinette Foundation, Medical Clinic, Hospital of the University of Pennsylvania.

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under such terms as pseudoreduplication of the second heart sound and telesystolic extracardiac sound, and (4) the systolic gallop rhythm later described by Potain.[3]

Potain's term, "systolic gallop rhythm," was a modification of Cuffer and Barbillon's "mesosystolic gallop," but in other respects he does not seem to have been greatly influenced by their discussion of the subject. Potain stated that the extra sound is heard best over the aortic area and is propagated to the carotids, but that it may be heard also over the entire precordium. He regarded it as an arterial phenomenon caused by diminished elasticity and tonicity of the aorta. He believed that aortic distention occurred quickly, but ceased suddenly with tension and shock which were responsible for the sound. He observed it in cases of typhoid fever, typhoid-like influenza, and "arteriosclerosis with aortic atheroma." Since Potain's paper, until recently, practically all writers on the subject have limited the diagnosis of systolic gallop rhythm to cases in which the extra sound resembled that described by Potain, and have agreed that it is not a common finding. In addition to the types of cases mentioned by Potain, it has been found to occur in such conditions as hypertensive cardiovascular disease and aortic insufficiency. We have been specially interested in the study of extra heart sounds for over ten years, and during this time have made the diagnosis of systolic gallop rhythm in eight cases.*

Recently, Thompson and Levine[4] published a clinical study of thirty-five patients who were said to have systolic gallop rhythm. They stated that the condition is frequent and that organic heart disease is usually absent. Johnston[5] reported twenty-one cases in which extra sounds occurred during cardiac systole and made sound tracings in all of these cases. He, like Thompson and Levine, called this grouping of sounds systolic gallop rhythm, although in the great majority of his cases the sound was loudest in the neighborhood of the apex and was described as a clicking sound. It would appear, therefore, that most of Johnston's cases fall in the group described by Gallavardin[2] as instances of reduplication of the second heart sound, or telesystolic extracardiac sound. Thompson and Levine state that some of their cases may be of this type.

We have tried to improve on Gallavardin's nomenclature by calling the sound described by him the "mid-systolic click."[6] Lian and Deparis[7] called it "Le Claquement meso-systoliques pleuropericardiale." Gallavardin believed that the sound was caused by tugging on pleuropericardial adhesions during systole, a view shared by Lian and Deparis, as is demonstrated by their nomenclature. Gallavardin's view has never been proved. Because of the sharp, clicking character

*Four of our patients with systolic gallop rhythm had aortic insufficiency, three, hypertensive cardiovascular disease, and one, miliary tuberculosis.

of the sound, variations in its time relations, depending on the phase of respiration, and lack of any clinical significance so far as the heart is concerned, we have long shared Gallavardin's belief that it is extracardiac in origin. We suggest, however, that it may be produced by the pressure of the contracting heart against some emphysematous area in the overlying lung.* Such a mechanism would account for the variations in its time relations, depending on respiration.

The mid-systolic click bears no resemblance to the systolic gallop described by Potain, except that both fall between the first and second sounds. The former is a click, or crepitating noise, not at all like an intrinsic heart sound. It is usually single, but may have two, or even three, components; it is usually heard best near the apex or over the body of the heart, but occasionally as high as the third intercostal space. It may be mid-systolic or near either the first or second sound. Although, as stated above, it has no significance as a sign of heart disease, it is occasionally found in a patient with heart disease.

We have discussed the common and clinically unimportant† mid-systolic click at such length because we believe it should not be classed as a form of systolic gallop rhythm or confused with systolic gallop rhythm.

So far as we are aware, the evidence for such an entity as aortic gallop of the type described by Potain has rested solely on auscultation. We wish to present supplementary objective data, based on graphic records, to help establish proof of the existence of this type of gallop rhythm.

We wish also to show that there may be, at the apex, a mid-systolic sound whose time relations with the first and second sounds and auscultatory characteristics are such that the grouping of sounds may be designated appropriately as apical systolic gallop rhythm.‡ In the one case observed, however, the extra apical sound occurred in conjunction with aortic systolic gallop rhythm. The apical sound was at first misinterpreted, i.e., was thought to be caused by propagation of the extra sound from the aortic area. However, sound tracings revealed differences in the time relations of the two, and over a small area both sounds could be recorded.

REPORT OF CASES

CASE 1.—E. P., a 21-year-old man, had old rheumatic heart disease and subacute bacterial endocarditis. Symptoms of the latter had begun to develop a few

*The sound can be imitated in the cadaver by pushing the heart against a subpleural emphysematous bulla. A similar sound is also heard in some cases of mediastinal emphysema.

†It becomes important only when it is mistakenly regarded as evidence of heart disease.

‡It is necessary to exclude splitting of the first or second sound, the semilunar opening click (to be reported), the mid-systolic click, frictions, murmurs, crepitations caused by air in the mediastinum, pleural space, or pericardium, sounds produced by auricular beats during ventricular systole, and all the sounds which may occur during ventricular diastole.

weeks before admission. The heart was greatly enlarged. At the apex a high-pitched, blowing, systolic murmur and a low-pitched, rumbling, diastolic murmur were heard. Over the aortic area there were a fairly loud systolic murmur, and a blowing diastolic murmur which began with the second sound. The physical signs were thought to indicate that he had mitral stenosis and insufficiency and aortic insufficiency. The pulse was of the Corrigan type, and a marked Traube pistol-shot sound and Duroziez murmur were present. The systolic pressure in the arms was 175. The diastolic pressure could not be obtained because of the loud pistol-shot sound. The patient grew worse rapidly as a result of the bacterial endocarditis. Four weeks after admission, Dr. F. C. Wood, while examining him, noted a mid-systolic sound, short in duration, and of about medium pitch, which was loudest over the base and gradually faded out over the body of the heart. Dr. Wood kindly called our attention to the sound. We observed that it was heard distinctly with all beats except extrasystoles; it was not materially influenced by respiration. It was heard with the patient in the sitting position and in various positions of recumbency, but best when he was supine. The pitch always seemed to be in the medium range. The patient remained in the hospital for eighteen days after this sound was discovered. During this period it was always found easily on auscultation.

The following studies were made: Sounds were recorded from the aortic area, the mid-sternal region, the xiphoid, and the apex, and were timed with the electrocardiogram. In addition, both the apex impulse and right carotid artery pulse were recorded optically in conjunction with the sounds and the electrocardiogram, care being taken to avoid parallax. Records of the Traube pistol-shot sound over the brachial and femoral arteries were made in conjunction with the electrocardiogram and a pulse tracing from the corresponding artery in the other limb (it had been ascertained previously that the two brachial pulses and the two femoral pulses, respectively, were synchronous).

CASE 2.—J. L., a man, 35 years old, developed aortic insufficiency at the age of 23, following an attack of rheumatic fever. Although he was somewhat handicapped physically by this lesion, he has been able to pursue his sedentary business occupation satisfactorily. In 1936, his physician, Dr. I. G. Klaus, sent him to Dr. Alfred Stengel for examination. Dr. Stengel noted what he regarded as systolic gallop rhythm at the aortic area, and kindly permitted us to listen to the sounds and make sound tracings. The patient was found to have considerable cardiac enlargement, systolic and diastolic murmurs at the aortic area, and an additional sound at the aortic area which occurred about midway between the first and second heart sounds. This extra sound seemed to be heard best in the first, rather than the second, right intercostal space. It was fairly loud and distinct, short in duration, and of about medium pitch. It was present with all beats, did not seem to be materially influenced by respiration, and was present both in the standing and recumbent positions. At the apex, there was a similar sound which was somewhat louder with the patient in the recumbent position. We assumed at the time that the sound heard at the apex was propagated from the aortic area. The blood pressure was 200/50. A Traube pistol-shot sound was present over the brachial artery.

The sounds over the aortic area were recorded in conjunction with the electrocardiogram and the right carotid pulse. Recently, through the kindness of Dr. Klaus and the patient himself, we were permitted to make further studies. The clinical findings were about as they had been the previous year. The mid-systolic sound was still present and had about the same characteristics; it was heard at both the aortic area and the apex.

The following studies were made: The sounds were recorded at the aortic area, the apex, and the mid-sternal region, in conjunction with the electrocardiogram.

Combinations of (1) sound tracing, right carotid pulse tracing, and electrocardiogram, and (2) sound tracing, apex cardiogram, and electrocardiogram, and (3) Traube pistol-shot sound over the brachial artery, brachial pulse tracing, and electrocardiogram were made. Parallax was avoided in all. Roentgenkymograms of the ascending aorta and the left ventricular border, each timed by an electrocardiogram according to a technique previously described,[8] were made.

In the two cases, the extra sounds were remarkably alike, except that in Case 2 the sound seemed to be heard well at the apex, although it was not as loud there as at the aortic area. The two cases were similar in that in both there was a well-developed aortic regurgitation, as well as a systolic murmur at the aortic region. The first patient, however, had more advanced aortic disease and mitral disease also, and was extremely ill because of his bacterial endocarditis. The second patient was in good health, and had no evidence of mitral disease.

Reference to Fig. 1*B*, Case 1, shows that the extra sound (*G*) fell just about midway between the first and second sound, and about 0.20 second after the beginning of the Q wave. The systolic murmur was quite conspicuous in the sound record prior to the extra sound, but was much less so after the sound (Fig. 1*A* and *B*). With ventricular extrasystoles, small mid-systolic vibrations were sometimes recorded even when we were unable to hear the sound in such beats (Fig. 1*C*). Following extrasystoles there was remarkable alternation in the amplitude of the recorded vibrations of the extra sound, although there was no perceptible alternation of the first sound (Fig. 1*C*). The time relations of the sound in successive beats were remarkably constant, which is in marked contrast to the time relations of a mid-systolic click. The extra sound began about 0.02 second after the peak of the carotid pulse wave (Fig. 1*B*). Fig 1*C* shows that there was a bifid apex impulse during systole. The extra sound, however, appeared to fall at the time of the trough between the two, and therefore was presumably not related to either wave.

Because of the fact that this patient had a well-marked Traube pistol-shot sound, it seemed worth while to try to ascertain whether the extra sound might be an analogous phenomenon, or, in other words, a pistol-shot sound originating in the aorta. It was found that the Traube sound in both the brachial and femoral arteries began with the local upstroke of the pulse wave (Fig. 4*B* and *C*). These observations indicate that the mechanism of the aortic, systolic, extra sound is not the same as that of the Traube pistol-shot sound, since the latter was synchronous with the beginning of the pulse wave at the point from which it is recorded, whereas the former came at a much later point on the aortic pulse (Fig. 1*B*). However, only one wave of sudden distention was recorded in the brachial and femoral sphygmograms, and this occurred at the very beginning of the pulse, whereas in the carotid pulse there was not only this initial wave of sudden distention, but also a secondary wave. Sound recordings just over the right subclavian artery

revealed a sound synchronous with the second wave of distention in the carotid. We thought, therefore, that the sound over the subclavian might be analogous to the Traube sound, in that it was synchronous with a wave of distention, although not, as in the case of the Traube sound, the initial wave of distention. The aortic extra sound, however, fell slightly later in the cycle. If, therefore, this sound were caused by sudden distention of the aorta, it would be necessary to assume that there was a secondary wave of distention in the aorta later than that in the carotid artery. Since it was not possible to make a roentgenkymogram of the aorta in this case, the results of the studies were not conclusive because

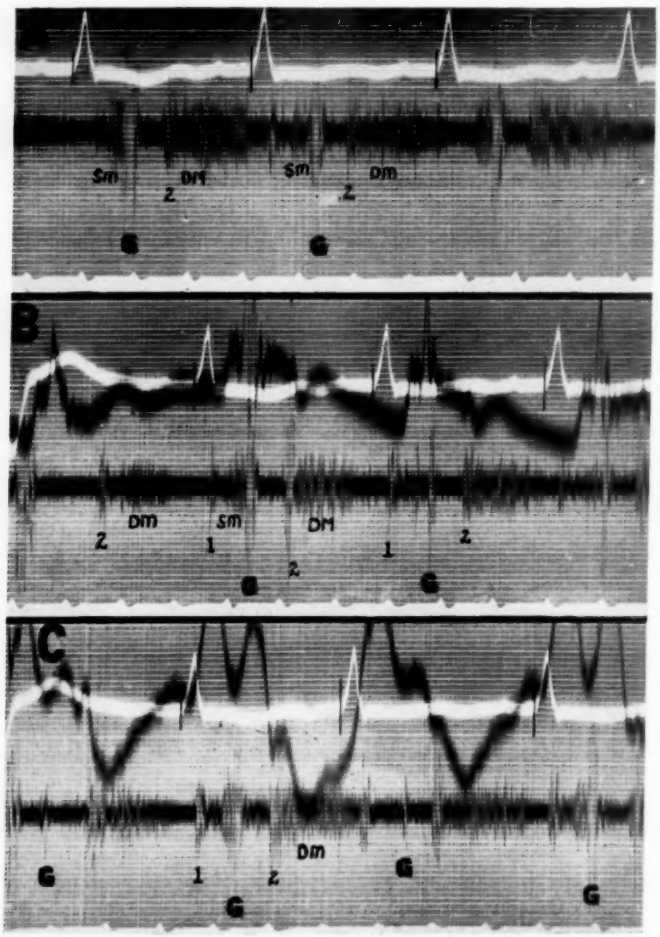

Fig. 1, Case 1.—*A*. Electrocardiogram and sounds recorded over the aortic area. There is an early systolic murmur, culminating in the mid-systolic (gallop) sound (*G*). A marked diastolic murmur begins with the second sound.

B. Electrocardiogram and sound and carotid pulse tracings. The extra sound occurs a little later than the sharp upward spike of the carotid tracing.

C. Electrocardiogram and sound and apex beat tracings. The mid-systolic sound falls in the trough between the two systolic peaks in the apex cardiogram. The post-extrasystolic alternation in this sound, and also in the second systolic wave of the apex cardiogram, is prominent. Parallax was avoided in all figures shown.

no direct evidence could be obtained to link the sound either with sudden distention of the aorta or with checking of the movement of distention.

In Fig. 2, Case 2, the sounds recorded at the first intercostal space just to the right of the sternum (*A*), the midsternal region (*B*), the fourth left intercostal space (*C*), and the apex (*D*) are shown. As in Case 1, the sounds recorded from the aortic area show an abrupt decrease in the magnitude of the systolic murmur following the sound recorded in mid-systole. The extra sound recorded from the fourth left intercostal space (*C*) clearly shows two components, the first beginning about 0.20 second after the beginning of the Q wave (the same time relation as in Case 1), and the other about 0.24 second after the beginning of the Q wave. The first component appeared to be caused by propagation of the aortic component, for the time relations were identical. For the same reason, the second component appeared to be caused by propagation from the apex. It was clear that the additional sound heard over the aortic

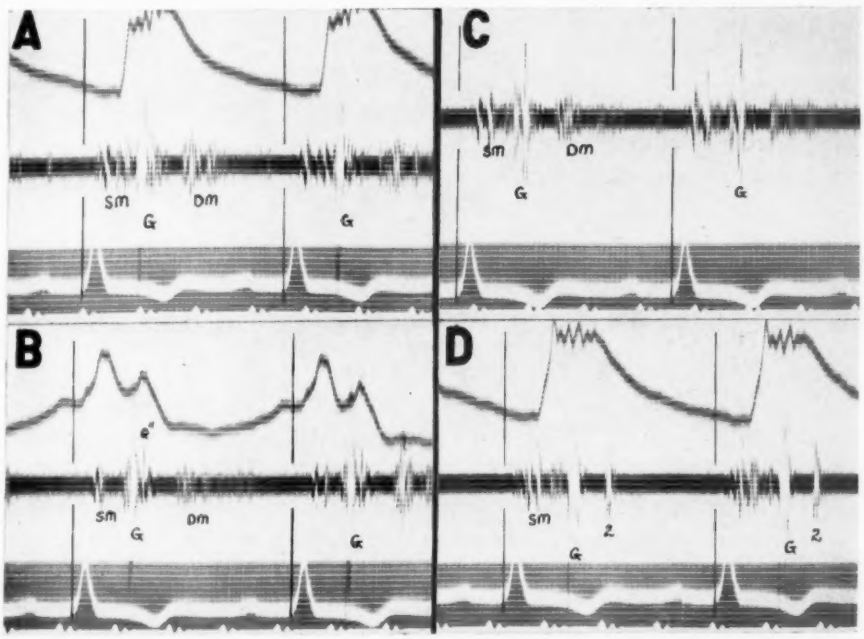

Fig. 2, Case 2.—*A*. Electrocardiogram, sounds recorded at first intercostal space just to right of sternum, and carotid pulse tracing. The mid-systolic (gallop) sound falls after the primary wave of distention of the carotid pulse, and just precedes a minor wave.

B. Electrocardiogram, sounds recorded from mid-sternal area, and apex cardiogram. At this position two extra sounds (*G* and *G''*) are recorded. The first corresponds in its time relations to the extra sound (*G*) recorded in *A*. It coincides with a point low on the ascending limb of the second systolic wave in the apex cardiogram. The second extra sound (*G''*), which at this area is represented by vibrations of much less amplitude than those of the first extra sound, occurs at the peak of the second systolic wave of the apex cardiogram.

C. Electrocardiogram, and sound tracing recorded from the fourth intercostal space just to the left of the sternum. At this area the vibrations of the second extra sound are much larger than those of the first extra sound.

D. Electrocardiogram, sounds recorded at the apex, and carotid pulse tracing. At this area the first extra sound was not recorded. The second is represented by vibrations of large amplitude.

area was not the same as the additional sound heard at the apex, since the different times of occurrence of the two made this impossible.

In Fig. 2*A*, it is noted that the extra sound, originating over the aortic area, does not correspond to the major wave of distention of the carotid, but does just precede a minor wave. A similar tracing (Fig. 3) had been obtained in this patient a year previously. The apex cardiogram (Fig. 2*B*) shows a bifid impulse during systole similar to that observed in Case 1. The additional sound, which was loudest in the aortic area, fell between these two waves and therefore did not appear to be related to them. However, the apical extra sound fell at the summit of the second wave (Fig. 2*B*, *G''*) in a manner similar to that in which the extra sound in diastolic gallop rhythm falls at the apex of a diastolic wave in the apex cardiogram.

A roentgenkymogram was made of the right edge of the ascending aorta and timed by an electrocardiogram (Fig. 5*A*). The contour of the aortic pulse, as judged from the roentgenkymogram, was considerably different from that of the carotid pulse. However, the roentgenkymogram records merely the resultant of movements parallel to the slit, which may be made up of movements caused by pulsation and of the aorta as a whole. Furthermore, the detail of extremely quick movements is apt to be lost because of the defects of roentgenkymography as a photographic method. The aortic gallop sound fell just about at the summit of the outward movement of the right border of the ascending aorta during systole (Fig. 5*A*, arrow); this movement appears to be caused mainly by the pulse wave. This would seem to relate the sound to checking of the distention of the aorta or to its impact against surrounding structures, rather than to the distention, per se, as in the Traube pistol-shot sound.

Roentgenkymograms of the left ventricular border did not help much in the attempt to explain the apical mid-systolic sound. The sound fell during a period of fairly quick inward movement of the ventricle (Fig. 5*B*). There was no wave on the kymogram corresponding to the second systolic peak of the apex cardiogram. It would appear, therefore, that the quick inward movement of the left border was accompanied either by a bulge of the anterior border or rotation of the heart, causing an impact which produced the second peak of the apex cardiogram.

DISCUSSION

Such data as we have been able to collect appear to support the view that the type of systolic gallop rhythm described by Potain is caused by the interpolation between the first and second heart sounds of an additional sound produced either by sudden checking of the movement of distention of the aorta or by its impact at that instant against surrounding structures. Its mechanism is therefore different from that of the Traube pistol-shot sound which is heard over the brachial, femoral, and,

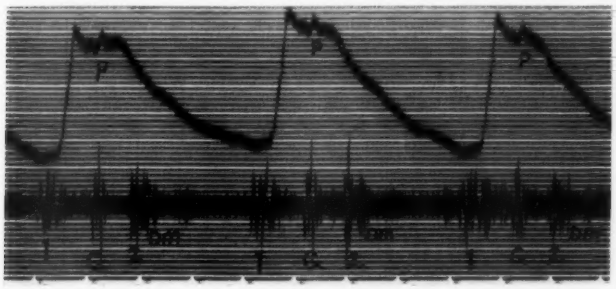

Fig. 3.—Electrocardiogram, carotid pulse tracing, and sound tracing from the aortic area, made in Case 2, one year prior to the records shown in Fig. 2. The relations of the mid-systolic extra sound and a minor wave in the carotid pulse (*P*) are similar to those shown in Fig. 2*A*.

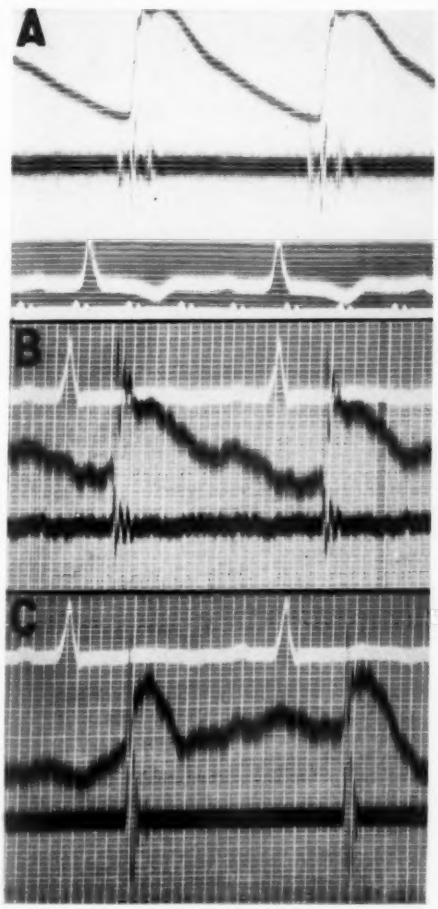

Fig. 4.—*A*. Case 2. Electrocardiogram, brachial artery pulse tracing, and sounds from the brachial artery. One group of sound vibrations preceded the pulse and were therefore presumably transmitted from above at a faster rate than the pulse wave. The second group is synchronous with the beginning of the pulse, and probably represents the Traube pistol-shot sound produced locally.

B. Case 1. Electrocardiogram, brachial artery pulse tracing, and sounds from the brachial artery.

C. Electrocardiogram, femoral artery pulse tracing, and sounds from the femoral artery. In both the brachial and femoral arteries the Traube pistol-shot sound was synchronous with the beginning of pulsation. In each instance the pulses were recorded in one extremity and the sounds in the other extremity, after it had been ascertained by means of simultaneous pulse tracings that the pulses were synchronous.

occasionally, the radial, arteries, since the latter sound is associated with distention of the vessels rather than checking of distention.

In experimental studies on heart sounds with the front of the chest opened, Wiggers[9] recorded directly over the aorta an additional sound whose time relations appear to correspond with those of the systolic gallop described by Potain. He states that sounds occurring at the semilunar valves tend to lose their characteristics on transmission through the chest wall, although he says that he did record the sound in a thin-chested child and was able to recognize it in a sound tracing of Battaerd's. He attributes the sound to the fact that the blood is ejected through the semilunar valves with increased velocity, setting the valves into vibration.

Whether or not the sound recorded by Wiggers in experimental animals is the analogue of the extra sound in the aortic systolic gallop rhythm observed in patients cannot be stated. If it is, the additional sound in gallop rhythm might be produced merely by exaggeration of a sound normally present but not loud enough to be transmitted through the chest wall. Such an increase in sound would result from (a) either unusually good transmission (Wiggers), or (b) forceful or sudden application of the dynamic factor concerned in its production. Wiggers' hypothesis concerning the mechanism of the sound observed by him would scarcely apply to the systolic gallop rhythm in our Case 2, since this sound came at the end of the period of maximum ejection.

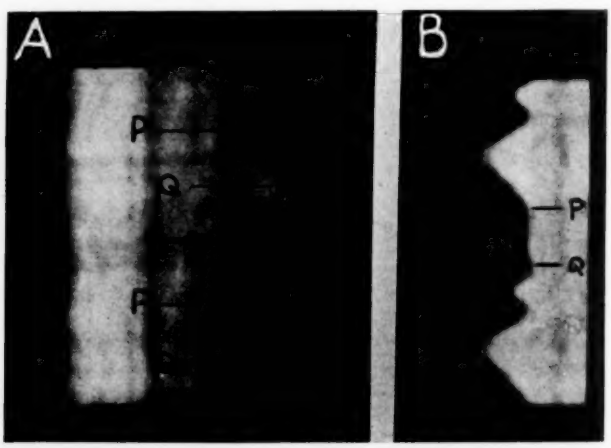

Fig. 5, Case 2.—The sequence is from top to bottom. *P* and *Q* refer to the beginning of the corresponding complexes in simultaneously recorded electrocardiograms.

A. Roentgenkymogram of the right border of the supracardiac shadow just above the heart. The patient was in the left anterior oblique position. The wave indicated by the arrow is caused by aortic movement during systole. The mid-systolic sound recorded over the aortic area, taking into account the heart rate, should fall at about the peak of this wave. The diastolic wave is unusual in kymograms made at this area. It is apparently not a venous pulsation, but is probably caused by rotation of the heart and pedicle.

B. Roentgenkymogram of the left ventricular border. The inward movement during systole is bifid. The apical extra sound occurs during the second and major inward movement. (See text.)

Just what the clinical significance of aortic systolic gallop rhythm may be cannot be decided until more cases in which its existence is proved are carefully studied. Our experience thus far would lead us to believe that it is most likely to occur in patients with well-developed aortic insufficiency. However, a similar sound occurs rarely in young individuals with severe infections, such as typhoid or typhoid-like fevers, and also in patients with hypertensive cardiovascular disease. Whether or not the mechanism is the same in these three types of cases remains to be decided.

The cause of the apical systolic gallop sound remains obscure. The fact that we have discovered it only in a case in which there was an aortic systolic gallop, and that it occurred only 0.04 second after the aortic gallop sound, suggests that the two were in some way related in this case. Furthermore, its coincidence with the peak of an apex impulse suggests that the actual mechanism of its production was by impact of the contracting ventricle against the chest wall. Such an impact might have resulted from the peculiarity in the pulsation of the aorta which had caused the aortic systolic gallop sound. We do not yet know whether apical systolic gallop rhythm may be independent of aortic systolic gallop.

SUMMARY AND CONCLUSIONS

1. Two cases of systolic gallop rhythm are reported, in which sound tracings and various other studies were made in the attempt to obtain evidence bearing on the mechanism of production of the extra sound.

2. It was demonstrated that there are at least two types of systolic gallop rhythm, exclusive of various other types of sounds which may fall between the first and second heart sounds.

3. In one of the types of systolic gallop rhythm, the additional sound is heard best over the aortic area. This type is termed aortic systolic gallop rhythm. In the other type the additional sound is heard best over the apical region; this type is termed apical systolic gallop rhythm. It has not yet been shown whether apical systolic gallop rhythm may be independent of aortic systolic gallop, although the time relations and position of maximum audibility indicate that their mechanism of production is not identical.

4. The additional sound in aortic systolic gallop rhythm appears to originate in the aorta. Its time relations suggest that it is caused by sudden checking of the distention of the aortic wall during systole, or by impact of the aorta against surrounding structures at that instant. It seems likely that either some abnormality of the heart beat or the aortic wall itself is necessary for the production of this sound. It has been noted particularly in cases of aortic insufficiency, typhoid or typhoid-like fevers, and hypertensive cardiovascular disease.

5. The cause of the additional sound in apical systolic gallop rhythm remains obscure. It is possible that impact of the cardiac apical region against the chest wall may be concerned in the mechanism of its production.

6. We think that it would be wise, for the present, to restrict the use of the term systolic gallop rhythm to conditions similar to those included under this designation by Potain.

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CARDIAC TOPOGRAPHY

Pathologic Studies of the Anterior Aspect of the Heart and Its Relationship to the Anterior Wall of the Chest in Common Heart Diseases

William Dressler, M.D.
New York, N. Y.

PERCUSSION gives, under favorable conditions, an approximately correct idea of the position, size, and shape of the heart. This information may be obtained much more clearly and precisely by roentgenologic examination. Yet, the roentgenogram, as Kienboeck[1] stated, is at best only a homogeneous "shadow picture" and can tell nothing of the "inner picture," i.e., of the elements that make up the shadow. Anatomic studies which were undertaken to fill this gap did not attempt to correlate the topography of the heart with the precordium.[2, 3] Such determinations are of importance for certain clinical questions.

The purpose of this study was to ascertain the contribution made by the chambers of the heart to the formation of its anterior wall under various pathologic conditions; and, furthermore, to determine their topographic relationship to the anterior wall of the chest. No attempt was made to study cardiac topography in the posterior or lateral aspects.

METHOD

The examinations were carried out on the cadaver, using a method which was suitable for demonstrating the natural topographic relations of the heart and its chambers to the anterior wall of the thorax. The principle involved consisted of the introduction of needles through the anterior wall of the chest along certain topographic lines, namely, the right and left sternal lines and the left midclavicular line. The needles were from 9.3 to 13.0 cm. in length, depending upon the thickness of the chest wall in those areas where they were to be inserted. They were pushed into the heart, whereby certain topographic areas of the anterior chest wall were delimited on the anterior wall of the heart. It was necessary for this purpose to insert the needles exactly vertically, parallel to one another. To insure this I used a specially prepared device with a plumb bob, which enabled me to insert the needles vertically through the anterior chest wall with the cadaver in the recumbent position. The second to fifth intercostal spaces in the right and left sternal lines, and the third to fifth intercostal spaces in the left midclavicular line were usually chosen as points of insertion. In some instances, needles were inserted elsewhere, as in the right midclavicular line when the heart extended far toward the right, or in the left parasternal line when the heart, as in emphysema, occupied a median position, so that the left border did not reach the left midclavicular line.

The needles were inserted immediately after death, in order to fix the heart in the position assumed immediately post mortem, and particularly to anticipate the onset of rigor mortis, which may begin as early as one-half hour after death. Since rigor mortis of the heart disappears within twenty-four hours,[4] I usually waited a little longer than that before carrying out my anatomic examination.

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The sites of insertion of the needles on the anterior chest wall, representing important points of orientation for further studies, were plotted with geometric precision. The thoracic layers were then removed one by one, care being taken not to disturb the position of the needles which remained fixed in the heart. After the skin was removed, the bony skeleton of the anterior chest wall was drawn into the diagram. Then those portions of the thoracic cage which covered the heart were sawed through and lifted over the needles, so that the lungs and the pericardium lay exposed. After the chest was opened the median borders of the lungs could retract but little, as they were fixed by the needles, and their position was drawn in the diagram. Finally, the pericardium was opened by a horizontal incision (along the margo acutus) and by a vertical median incision. The two lamellae were lifted off the needles and, together with the adjacent borders of the lungs, laid back and sutured to the lateral wall of the chest. The anterior wall of the heart and the intrapericardial portions of the large vessels now lay open. It was easy to measure (by means of calipers) the various sections of the heart and vessels in natural size, and to draw in the contours. The relation of the heart to the anterior chest wall was fixed by the original orientation points, as indicated by the inserted needles.

A total of twenty-five cases of heart disease, in all of which careful clinical studies had been made, were examined by this method.* Various diseases of the heart were present, including isolated and combined valvular lesions, myopathies, and cor pulmonale. Among the valvular lesions there were four cases of pure mitral stenosis, one of uncomplicated mitral regurgitation, and three of syphilitic aortic regurgitation; in five cases there were combined valvular lesions, in two of which a marked degree of aortic stenosis was the predominant lesion. The cor pulmonale group included three cases of pulmonary emphysema and one case of marked pleural thickening. Among the myopathies were various diseases; there were one case of thyrotoxicosis, three cases of coronary sclerosis with aneurysm of the ventricles, two of hypertensive cardiovascular disease with coronary sclerosis, and, finally, two cases of myopathy of unknown etiology.

NORMAL TOPOGRAPHY

Since normal hearts were not available for my study, information was obtained from the texts of Luschka,[5] Corning,[6] Toldt,[7] and Tandler.[8]

The heart is divided through the median plane into two unequal sections (Fig. 1); two-thirds of the heart lies to the left of the midsternal line, and one-third to the right.

Right atrium.—The right atrium (Fig. 1) is largest in a craniocaudad direction and extends from the third to the sixth costal cartilage. It lies almost entirely in the right half of the chest, with only the tip of the auricular appendage extending a little to the left of the midline at the level of the third rib. From this point the median border of the atrium passes obliquely to the right margin of the sternum, which it joins at about the level of the fifth chondrosternal junction. The outer border of the right atrium (the right border of the heart) is about a thumb's width (1 to 2 cm.) to the right of the right margin of the sternum.

Right ventricle.—The right ventricle (Fig. 1) constitutes the greatest portion of the anterior wall of the heart, about two-thirds of its surface. This area is approximately triangular in shape; the base is formed by the margo acutus, which also forms the lower border of the heart. This usually lies at the level of the

*These studies were made in the department of pathology of the hospital of the Wiener allg. Poliklinik.

attachment of the xyphoid process to the sternum. The right border of the ventricle (corresponding to the already described line of the median contour of the right atrium) usually does not extend beyond the right border of the sternum and does not participate in the formation of the right border of the heart. The left border of the right ventricle is formed by the anterior longitudinal sulcus, which passes obliquely from the third left rib, near the chondrosternal junction, to the fifth intercostal space. Here it extends a little beyond the left parasternal line and is about 5 cm. distant from the left border of the sternum. The uppermost part of the right ventricle, the conus arteriosus, lies at the level of the third intercostal space, with a narrow section behind the left half of the sternum and a wider portion extending considerably beyond the left border of the sternum.

Left atrium.—The tip of the left auricular appendage is the only portion of the left atrium which is visible in the anterior aspect (Fig. 1); it is found at the level of, and a little above, the sternal attachment of the third left rib.

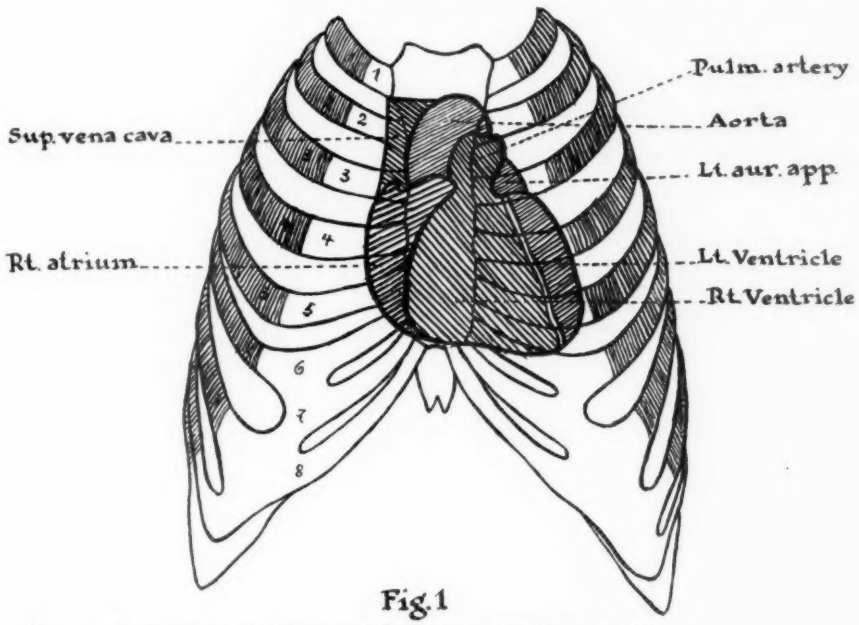

Fig. 1.—Topography of the normal heart (modified from Toldt).

Left ventricle.—Under normal conditions, only a narrow area of the left ventricle, about as wide as a thumb, can be seen from the front (Fig. 1). It extends from the third left costal cartilage to the fifth intercostal space, and it normally forms almost the entire left border of the heart and the apical area. Luschka[5] has stressed the fact that the anterior longitudinal sulcus is not actually the right border of the left ventricle, because the interventricular septum bulges far into the cavity of the right ventricle. The right border is at least a thumb's width nearer the midline and almost reaches the left border of the sternum in the vicinity of the third and fourth ribs.*

*Keith,[2] in a recent anatomic study, has questioned some of the statements of the anatomists regarding the elements constituting the anterior aspect of the normal heart. According to his investigations, the left auricle is rarely visible in front of the heart. The conus pulmonalis often participates in the formation of the upper third of the left cardiac border, while the pulmonary artery not seldom fails to appear in the anterior aspect of the heart.

Large Vessels.—The ascending aorta, which originates at the level of the third intercostal space behind the left half of the sternum, is visible anteriorly at about the level of the third rib (Fig. 1); thence, occupying the entire width of the sternum (except for a narrow border at the left) it passes to the manubrium sterni, where it turns to the left. The projection of the trunk of the pulmonary artery on the anterior thoracic wall extends from the attachment of the second to the attachment of the third left costal cartilage and corresponds to the anterior end of the second left intercostal space and to a narrow adjacent portion of the left half of the sternum. The trunk of the pulmonary artery normally rises almost vertically, a fact which must be noted particularly in considering pathologic conditions. The superior vena cava lies to the right of the sternum, and extends from the third rib to the sternal end of the first intercostal space.

It is hardly necessary to point out that all statements concerning the topography of the heart and vessels must be schematic and general, for the position and shape of the heart and, hence, its anterior aspect are influenced by several factors, varying from case to case. The position of the diaphragm is important, as is the pull of the lungs on the pericardium (Tandler[8]).

PATHOLOGIC CHANGES

GENERAL LAWS

Pathologic deviation from the normal in the configuration and topography of the heart, disregarding the effect of external factors (hydrothorax, tumors, abnormally high position of the diaphragm, etc.), are, in general, caused by changes in the size of the whole heart, or of its various portions. It is usually difficult to decide to what extent hypertrophy or dilatation accounts for enlargement of the heart, particularly because these two pathologic conditions usually occur together. According to radiologic studies, pure hypertrophy usually causes a change in the shape of the heart, but no appreciable enlargement of the roentgenologic silhouette. The latter is caused principally by dilatation of the cardiac cavities.

Isolated enlargement of a single section of the heart was scarcely ever found in the terminal stages of those heart diseases which were studied anatomically. A combination of enlargement of several cavities was the rule. In order to understand the anatomic findings it is important to bear in mind the fact that changes in one section of the heart exert an effect on the shape and topography of adjacent portions, displacing them from their normal position and distorting their contours. For instance, enlargement of the right ventricle may be simulated when the latter is encroached upon from behind by an adjacent, dilated chamber, and so is forced, vicariously, to dilate in a transverse direction.

It may be said, in general, that enlargement of the heart is limited in certain directions by the configuration of the chest and by the structure of neighboring organs. The rigid walls of the chest soon inhibit extension of the heart in an anteroposterior direction. Caudad, the resistance of the tense diaphragm, re-enforced by the liver, rarely al-

lows cardiac expansion of a considerable degree. Enlargement of the heart often develops cephalad, but is most common laterally because yielding lung tissue is easily displaced. The dilatation in a lateral direction provides particularly favorable conditions for demonstrating pathologic enlargement of the heart in the anterior aspect. The direction of enlargement is also determined by the type of fixation of the heart. Three factors in particular, according to O. Stoerk,[10] are important: First, there is the firm, immovable attachment of the inferior vena cava to the diaphragm. The very short, intrathoracic portion of the inferior vena cava permits some excursion, though this always involves kinking in the region where it passes through the diaphragm. The second is the fixation, dorsad, of the descending aorta by the intercostal arteries. The third is the fixation of the pericardium to the diaphragm.

The direction of enlargement and the configuration of the various sections of the heart under certain pathologic conditions can be best discussed by citing characteristic cases.

A. Heart Diseases With Predominant Participation of the Right Half of the Heart

1. MITRAL STENOSIS

Case 1. Buttonhole stenosis of the mitral valve. The patient was a man, 31 years of age, who weighed 50 kg. He was of medium size and had a slender bony structure, with a long, rather flat thorax.

Clinical cardiac findings.—The precordial area was bulging, and the apical thrust was not visible. In the fifth intercostal space, about 1.5 cm. within the left midclavicular line, there was a distinct, circumscribed, systolic retraction of the soft tissue. Mesiad, the precordial region showed a large systolic elevation, most marked along the left border of the sternum between the fifth and sixth ribs. This pulsation extended about 5 cm. to the left of the sternum; on the right side of the sternum, particularly in the lower portions, a section about 2.5 cm. in diameter was raised during systole. The liver could not be palpated.

Percussion: The cardiac dullness extended about 3.5 cm. beyond the right border of the sternum; the lower third of the sternum gave an absolutely flat note. To the left of the sternum, in the third intercostal space, there was a zone of increased dullness, measuring 3.5 cm.

Auscultation: Over the apical portion there were a presystolic crescendo murmur, a high-pitched first sound, and a rumbling diastolic murmur. At the base, on either side of the sternum, a faint first and a loud second sound were heard.

Autopsy findings (Jan. 6, 1931; No. 5/ 1931).—The right ventricle was enlarged and bulging and formed the apex of the heart. The trabeculae and papillary muscles of the right ventricle were widened. The left ventricular cavity was not dilated; its wall measured as much as 0.7 cm. in thickness. The left atrium was very large and its wall was thickened; the right atrium was also dilated; its wall was not thickened. The aorta above the ring measured 6.5 cm., the pulmonary artery above the ring 7.0 cm. The two cusps of the mitral valve were fused and formed a rigid ring with a buttonhole opening; the edges of the leaflets were thick, corded, and studded with calcified, warty excrescences. The chordae tendineae were thickened and somewhat shortened. The aortic and pulmonary cusps were normal. There was a slight adhesion between two leaflets of the tricuspid valve. The ostium of this valve was not appreciably narrowed.

Anterior aspect of the heart (Fig. 2).—The entire heart was enlarged transversely mainly because of dilatation of the right ventricle. Its extension to the left displaced the anterior longitudinal sulcus beyond the left midclavicular line, so that only a very small portion of the left ventricle participated in the formation of the anterior wall of the heart, constituting the caudal part of the left border. The greater, cranial section of the left border was formed by the convexity of the dilated right ventricle. The left auricular appendage was not visible. The apex of the heart was formed by the right ventricle. There was only slight enlargement of the right ventricle to the right and cephalad, but the lower border of this chamber was almost the width of an intercostal space further caudad than normal; it apical portion corresponded to the sixth left intercostal space. The right atrium was somewhat elongated in the craniocaudad direction, and was notably widened, extending twice the normal distance beyond the right border of the sternum. The tip of the right auricular appendage was shifted to the left, and approached the left margin of the sternum in the third intercostal space. The visible portion of the superior vena cava was dilated; the pulmonary artery was somewhat larger than the aorta and, in contrast to its normal direction, pursued an oblique course medially and cephalad.

Before death a mark was placed at the point near the apex where a circumscribed systolic depression of the soft tissues was observed. A needle inserted at this point immediately after death pierced the heart somewhat cephalad of the apical portion, about 3 cm. from the left and 3 cm. from the caudal border of the heart (Fig. 2*E*).

The anterior wall of the heart in the presence of right-sided cardiac enlargement.—Dilatation of the right ventricle and right atrium gives, in cases of mitral stenosis, a distinctive character to the anterior aspect of the heart. Hence these examples are especially suited for the study of the most important characteristics of dilatation of the right-sided cavities of the heart. The anatomic findings may also serve to clarify some of the radiologic observations.

Right atrium: Enlargement of the right atrium, as noted in the anterior view (Fig. 2), results especially in an increase in the transverse diameter, so that its outer border may extend 4 to 6 cm. beyond the sternum. On the medial aspect, the dilatation of the right atrium is usually blocked by the right ventricle, which is ordinarily also enlarged. The right auricular appendage rarely reaches the left border of the sternum, and only exceptionally does it extend to any considerable degree beyond this. The atrium scarcely ever extends appreciably cephalad, but sometimes the caudal portion of the right atrium dives deep into the epigastric angle. This is particularly true in cases of tricuspid regurgitation, the lesion which usually causes the greatest degree of dilatation of the right atrium.

Bulging of the right atrium produces a marked rounding off of the contour of the right side of the heart and an increase in its extent to the right of the midline, as is well known to the radiologists. These changes, however, when observed on roentgenologic examination, cannot be taken as definite evidence of enlargement of the right atrium, for, under certain conditions, the right ventricle may be encroached upon from behind by an enlarged left ventricle and extend to the right of the sternum. This displaces the right atrium posteriorly and to the

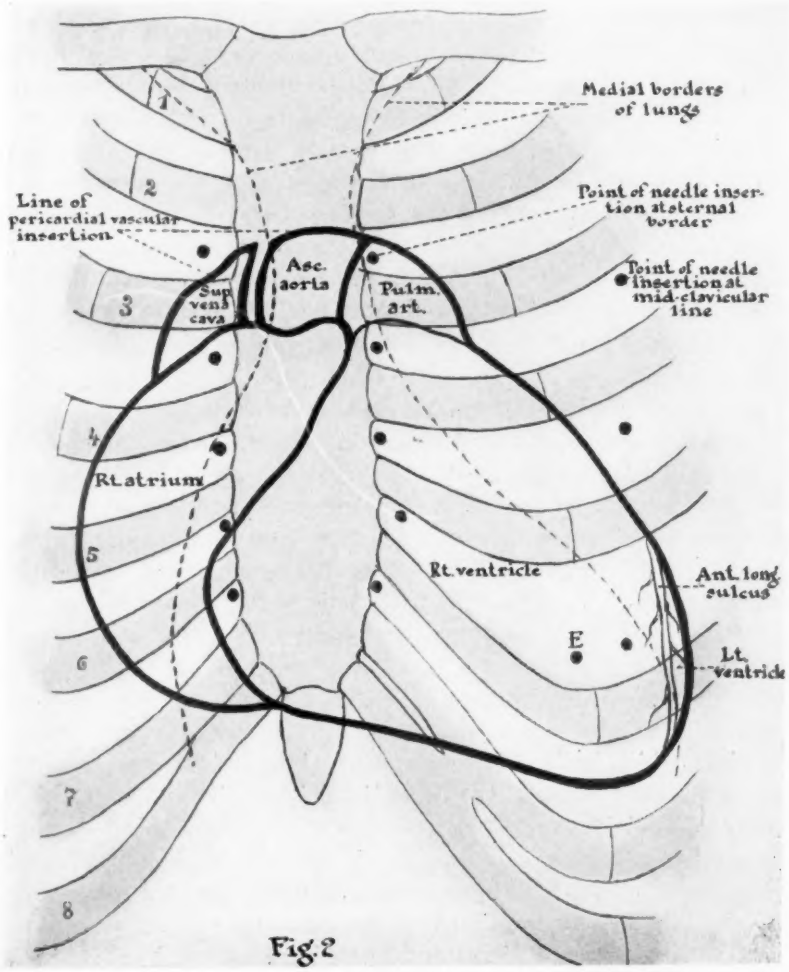

Fig. 2, Case 1.—Buttonhole stenosis of the mitral ostium. The circular dots show the insertion of the needles: in the right and left sternal line (second to sixth intercostal space), and in the left midclavicular line (third to fifth intercostal space). Only the intrapericardiac portions of the big vessels are drawn.

The right atrium and right ventricle are enlarged in the transverse diameter. Only a small strip of the left ventricle is visible. "Mitral configuration" of the heart is present.

right, so that only a narrow section of the latter chamber remains visible from the front (see Figs. 6 and 8). Thus, the right median distance is

increased, and the right border of the heart is markedly curved outward without enlargement of the right auricle. On the other hand, the right atrium may be pressed ventrad against the chest wall by a greatly dilated left atrium, so that it increases in width and appears enlarged in the anterior aspect.

Furthermore, it has been shown[9] that, as the whole heart rotates counterclockwise (seen from above) because of right ventricular enlargement, the right atrium is displaced forward and to the left. A greater portion of this chamber is visible than in the anterior aspect. This is particularly true in cases of marked tricuspid regurgitation, as will be pointed out later (see Fig. 4).

Right ventricle: Distention of the right ventricle occurs primarily to the left and also somewhat cephalad. This involves a twisting of the entire heart around its longitudinal axis in a counterclockwise direction, i.e., from right to left and dorsad, as seen from the anterior aspect. Not only the left ventricle, but also the left atrium is displaced dorsad. The left atrium is also displaced to the right, thus forcing the right atrium ventrad and to the left. Because of the enlargement of the right ventricle, the anterior longitudinal sulcus moves outward, so that the left ventricle may occasionally disappear entirely from the anterior aspect.

In the majority of cases, however, a narrow segment of the left ventricle remains visible and participates in the formation of the lower half of the border of the heart. The greater part of the left border, however, is formed by the right ventricle, and particularly by the dilated conus arteriosus, which bulges outward and bridges the "waist of the heart" which normally lies between the large vessels and the ventricular border. This causes the pathologic contour which we recognize roentgenologically as "the mitral configuration." This peculiar shape of the heart, regularly observed in the presence of mitral lesions, was originally attributed to two factors:[11] (1) Dilatation of the left atrium, and (2) dilatation of the pulmonary artery. It was suggested that the left atrium, which is dilated as a result of mitral lesions, presses ventrad, and fills out the "waist of the heart." This opinion, which dominated the views of clinicians for a long period, was later contested by Assmann,[9] who found from anatomic studies that it was not the dilated left atrium but the dilated conus arteriosus which produced the "mitral configuration." At the most, according to Assmann, only a narrow segment of the left atrium which adjoins the dilated conus can be seen in such cases. This view is substantiated by my own anatomic studies, and I may add that I have *never* found the left atrium, but always the dilated conus of the right ventricle, forming the upper left border in these cases. The left atrium becomes part of the anterior wall when it is excessively dilated and may participate in forming the right, rather than the left, border. Only exceptionally has it an appreciable share in the left cardiac outline.[3]

Insofar as the pulmonary artery is concerned, its contribution to the development of the "mitral configuration" appears to be a matter of altered course, rather than of dilatation of the vessel proper. As the conus arteriosus dilates to the left, the attachment of the pulmonary artery moves outward too, so that the pulmonary artery, in order to reach toward the midline, must take an oblique course from the left ventrad to the right dorsad direction. Hence, its outer border, together with the border of the dilated right ventricle, forms an oblique line, which, when the conus arteriosus is greatly enlarged, bulges outward in a manner corresponding to that of a roentgenologically visible third left arch. In such cases the angle between the aortic arch and the left ventricular contour is filled, and thus the "waist of the heart" disappears.

Since the normal rounding of the left border of the heart is produced by the left ventricle, the more the left ventricle is displaced dorsad, and the less it participates in the formation of the anterior wall of the heart, the steeper the lower half of the left border appears. The steepest course was seen in cases of tricuspid regurgitation in which the left border was formed entirely by the right ventricle (see Fig. 4). From what has been said, it can be seen that with marked dilatation of the right ventricle the apical portion of the heart is also formed by this chamber.

Considerable enlargement of the right ventricle may displace its lower border as much as 2 cm. caudad of the base of the xyphoid process. In experiments on frozen cadavers it has been found[12] that with mitral lesions the caudal border of the heart may be lowered by as much as the vertical diameter of one vertebral body.

Usually, the right ventricle is not dilated to the right. This is commonly explained by assuming that the right atrium, which is fixed to the diaphragm by the inferior vena cava, prevents any extension of the right ventricle in this direction. This explanation does not seem to be valid, for we have seen that the right ventricle, under certain circumstances, i.e., when impinged upon from behind by the dilated left ventricle, may extend to the right of the sternum for a considerable distance. Hence, there must be another reason for the undoubtedly correct observation that the right ventricle dilates primarily to the left. Kirch[13] has shown that the outflow tract of the ventricles is the first part to undergo hypertrophy, as well as dilatation, particularly the portion below the origin of the large arteries, i.e., for the right ventricle, the conus pulmonalis. Since the outflow tract of the right ventricle is situated much to the left, it will be understood why enlargement of this ventricle occurs primarily toward the left, especially in cases of mitral stenosis, when the left ventricle is atrophic and thus offers little resistance to displacement by the right ventricle. Dilatation and hypertrophy advance in the opposite direction to the flow of blood, that is, from the outflow tract toward the inflow tract.[13] If failure, with dilata-

tion of the right ventricle, has taken place, it is soon followed by distention of the right atrium, which then interferes with any extension of the right ventricle to the right, so that the ventricle is forced to continue its original direction of distention toward the left.

2. COR PULMONALE (PULMONARY EMPHYSEMA)

CASE 2. This was a case of "emphysema heart" in a man, 51 years of age, who weighed 60 kg. and was 168 cm. tall. He had a moderately heavy bony framework, with but a slight panniculus adiposus.

Autopsy (Dec. 13, 1933; No. 164/1933).—Chronic pulmonary emphysema. The right ventricular cavity was considerably dilated. The anterior wall of the ventricle bulged, and the rounded apical portion of the heart was formed by the right ventricle. The left ventricle was relatively small, its wall measuring no more than 2.0 cm. in thickness. The papillary muscles and the trabeculae of the right ventricle were very heavy; the tricuspid leaflets and pulmonary cusps were normal; the right atrium was markedly dilated, and the left was normal.

Anterior aspect of the heart (Fig. 3).—Two features pointed to the presence of pulmonary emphysema. 1. The median borders of the lungs met almost in the midline; they could not retract after the chest was opened, since they were fixed in position by the needles inserted along the borders of the sternum. 2. The whole heart occupied a low position, with the lower border about 3 cm. caudad to the base of the xyphoid process.

The most marked finding was again the enlargement of the right ventricle, which, together with the right atrium, dominated the anterior aspect of the heart. The entire left ventricle was displaced dorsad, and all of the left border of the heart was formed by the enlarged right ventricle. The needle which was inserted in the fifth intercostal space in the left midclavicular line met the anterior longitudinal sulcus exactly at the left border of the heart (Fig. 3*S*). This is the most impressive evidence of the marked right ventricular enlargement, for the low position of the diaphragm in itself would tend to rotate the heart around its longitudinal axis from left to right (seen from the front); hence, in the absence of right ventricular enlargement, a large part of the left ventricle should appear on the anterior aspect. The right atrium was moderately enlarged, but distinctly dilated in the longitudinal direction. Nothing abnormal was found in the large vessels.

3. TRICUSPID REGURGITATION

Case 3.—Extreme tricuspid incompetence of muscular origin in a case of myopathy of unknown etiology.* The patient was a man, 59 years of age, who weighed 62 kg. He was of medium size, and had a slender bony framework, meager musculature, and a moderately wide thorax.

*A detailed description of the clinical findings and the results of roentgenologic examination are given in this case because the extremely interesting symptoms are especially illuminated by the anatomic picture. The case was reported from the clinical standpoint by Dr. Robert Fischer, in Wien. klin. Wchnschr. **41**: 657, 1928, and **46**: 1545, 1938. The peculiar pulsatory phenomena in this case were evaluated by W. Dressler in the Monograph: Die Brustwandpulsationen als Symptome von Herz- und Gefaesskrankheiten, Wien, W. Maudrich, 1933.

Clinical findings.—There was very marked cyanosis of the face and the tips of the fingers. Slight edema of the legs was present. The greatly dilated cervical veins showed an excessive degree of systolic pulsation. The diameter of the internal jugular vein was twice that of a thumb. The ear lobes moved noticeably during systole as a result of the pulsation transmitted from the adjacent veins. The veins of the thorax and upper extremities were also greatly dilated.

Clinical cardiac findings.—The region of the heart bulged slightly. With each systole the entire chest underwent a jerky shift from left to right. This movement was formed of two components, namely, (1) a diffuse, extraordinarily distinct systolic depression of the precordial area, even of the entire left half of the chest, and (2) a less marked outward bulge of the right side of the chest, likewise systolic in time. The latter pulsation was most marked in the region of the liver and decreased in intensity craniad to the sixth rib. If one palpated the heart area with the right hand, while the left lay over the liver area, a distinct seesaw movement was discernible, in that the right hand sank during systole, while the left hand was raised. A forcible propulsion was felt over the precordial area during diastole. No localized apical impulse was found.

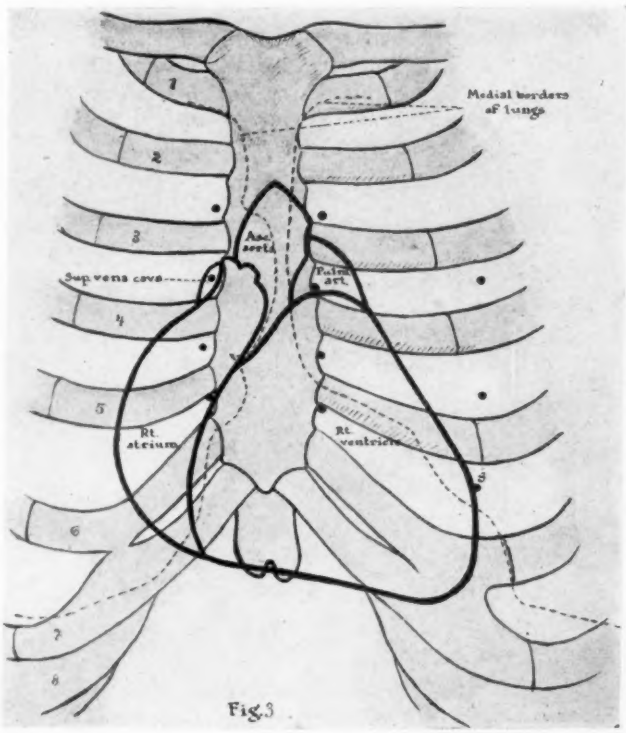

Fig. 3, Case 2.—"Emphysema heart." The median borders of the lungs meet almost in the midline. The heart is displaced caudally. The right ventricle is dilated to the left. No part of the left ventricle is visible. The needle inserted in the fifth intercostal space in the left midclavicular line met the anterior longitudinal sulcus at the left border of the heart (*8*).

Percussion: The cardiac dullness extended to the right about 5 cm. beyond the right sternal border. The lower end of the sternum was absolutely flat.

Auscultation: The first sound at the apex was very faint; the second sound was distinctly double, and the second component coincided exactly with the diastolic propulsion of the thoracic wall. The heart sounds at the base were scarcely audible.

The liver extended 7 cm. below the costal margin in the right midclavicular line; it was prominent and showed an extraordinarily strong systolic expansile pulsation.

Roentgenological findings (Dr. H. Roesler).—The heart was markedly enlarged to the right and left. The transverse diameter measured 20 cm. The left border of the heart showed pulsations of large amplitude, particularly near the base. There was a distinct systolic inward movement of the right border, particularly well marked near the diaphragm; on the whole, however, the amplitude was considerably smaller here than on the left side. The aortic pulsations were of small amplitude, which was in pronounced contrast to the large pulsations of the left heart border; this permitted one to conclude that the latter was formed by the right ventricle.

Autopsy findings (Feb. 9, 1932; No. 19/1932).—Marked right ventricular hypertrophy and dilatation, with incompetence of the tricuspid valve, were present. Upon opening the pericardium the greatly enlarged right ventricle presented. The left ventricle was entirely on the dorsal surface. The apical portion of the heart was formed by the right ventricle. The right atrium was large, and formed a sac almost the size of a fist. The left atrium was small. The cavity of the right ventricle was very large; its walls were moderately thickened, measuring, at most, about 0.7 cm. The endocardium showed spots of a glistening and callous appearance. There was widening of the tricuspid ring; the ostium easily admitted four fingers. The border of the anterior cusp of the tricuspid valve was very jagged and rolled. The borders of the two other cusps were delicate, thin, and transparent, showing only linear thickenings on the cusp adjacent to the wall. The chordae tendineae were delicate and thin. The wall of the right atrium was thin. The pulmonary cusps were normal. The pulmonary artery above the ring measured 7.5 cm. The mitral and aortic valves were perfectly normal. The aorta above the ring measured 8 cm. The ostia of the coronary arteries were patent; the left coronary artery was of adequate size, with some dense plaques in its initial portion. The intima of the ascending aorta was smooth and glistening; some fatty and calcified plaques were present in the arch. There were some fatty plaques in the descending thoracic aorta. The wall of the abdominal aorta was rigid and, in places, calcified.

Microscopic findings: Heart: no changes were found either in the ventricular or atrial myocardium. Lungs: sections from all lobes revealed no sclerotic changes in the branches of the pulmonary artery. Purulent bronchitis was present.

Anterior aspect of the heart (Fig. 4).—The right atrium and the right ventricle were excessively dilated; hence, the rotation of the heart around its longitudinal axis (from right to left in the anterior aspect) was particularly marked. The left ventricle was forced completely dorsad; the normal curve of the left border of the heart was absent; the left border of the heart pursued a rather steep course, extending from the third rib to the upper border of the seventh rib. The apical portion of the heart was displaced downward and was formed by the right ventricle. The right atrium was of enormous size, especially dilated in the transverse diameter. It extended 6 cm. to the right of the right border of the sternum, about three times the normal distance, so that the right border of the atrium came very close to the right midclavicular line. The right auricular appendage was shifted to the left, and touched the left border of the sternum at the level of the fourth rib. The marked rotation of the entire heart to the left was also evidenced by the fact that the sulcus terminalis, which normally is on the lateral wall of the right

atrium, and therefore invisible from the front, was here forced forward, so that it was visible in the anterior aspect. Likewise to be attributed to the rotation of the heart was the fact that the pulmonary artery was displaced dorsad, so that only a small portion of the stem of the artery could be seen from the front. The marked dilatation of the superior vena cava was noteworthy. In the caudal direction the heart appeared to be only moderately dilated.

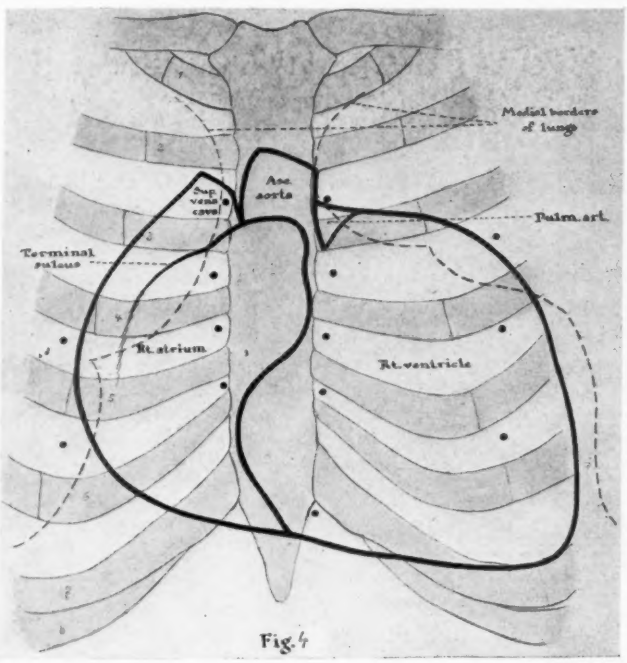

Fig. 4, Case 3.—Extreme tricuspid regurgitation. On account of the considerable extension of the heart to the right, needles were also inserted in the right midclavicular line in the fourth and fifth intercostal spaces. Tremendous enlargement of the right auricle and right ventricle in a transverse direction. Left ventricle not visible. Note the steep course of the left border of the heart. The terminal sulcus is visible in the anterior aspect of the right auricle.

The anatomic picture substantiated the assumption of the roentgenologists that the left border of the heart in this instance was formed by the right ventricle. It also gives us a better understanding of the pulsatory phenomena which are observed at the left side of the chest in many cases of tricuspid regurgitation. The marked systolic diminution in size of the abnormally large right ventricle cannot be equalized by a corresponding increase in the volume of the lungs, which are displaced laterally and are partly atelectatic. Hence, during systole, the anterior and the lateral left chest wall is depressed by atmospheric pressure; the diffuse systolic depression of the left half of the thorax which results is characteristic of many cases of tricuspid regurgitation.[14, 15, 16] If one were to overlook the systolic pulsation of the liver, confusion might re-

sult because of the fact that similar pulsatory phenomena occur in adhesive pericardial disease.

4. MITRAL REGURGITATION

Uncomplicated mitral regurgitation is rare, particularly as the sole cause of death. I have had the opportunity to study one such case anatomically.

CASE 4.—Uncomplicated mitral regurgitation. The patient was a man 28 years of age, who weighed 77 kg. He was very tall and slender, of strong build, with moderately developed musculature.

Clinical cardiac findings.—There was a distinct precordial bulge. The apical thrust was in the sixth intercostal space, almost in the anterior axillary line, wide, heaving, and vigorous. The lower sternal area was completely flat on percussion. The cardiac dullness on the right extended 1.5 cm. beyond the right border of the sternum. To the left and craniad, in the third intercostal space, there was a broad zone of increased dullness which extended from the sternum almost to the left midclavicular line. Auscultation revealed a distinct gallop rhythm all over the heart, and a rough systolic murmur at the apex. The pulmonic second sound was accentuated.

Autopsy findings (Oct. 30, 1931; No. 154/1931).—The heart was enlarged. The left ventricular cavity was markedly dilated; its wall measured as much as 1.5 cm. in thickness. The mitral valve was thick and corded on the free margin; the chordae tendineae were shortened and thickened. The mitral orifice was not narrowed. The aortic cusps were normal. The left atrium was dilated, and its inner surface was smooth. The intima of the aorta was smooth and glistening throughout. The right ventricular cavity was dilated; its wall measured as much as 0.7 to 1.0 cm. in thickness; the tricuspid valve was normal. The right atrium was spacious. The pulmonary cusps were normal. The pulmonary artery above the ring measured 8.5 cm., the aorta, 8.0 cm.

Anterior aspect of the heart (Fig. 5).—The right ventricle was dilated, particularly to the left and cephalad, where the conus arteriosus bulged markedly outward. The trunk of the pulmonary artery continued this arch, and its course toward the median line was almost horizontal. The left atrium was invisible. The left border of the heart was formed largely by the right ventricle; the left ventricle participated only along the lower half of the heart, where it formed a moderately large segment of the anterior wall. The whole heart appeared to be enlarged longitudinally; the apical portion lay at the sixth intercostal space and was slightly lengthened. Although the pulmonary artery was found to be larger than the aorta at autopsy, the anterior aspect of the heart showed the opposite condition because of the rotation of the whole heart to the left, whereby the pulmonary artery was partly displaced dorsad. The superior vena cava was moderately dilated.

This picture of mitral regurgitation, which is characterized by the "mitral configuration," as is mitral stenosis, differs in some aspects from the latter. This is apparently because left ventricular hypertrophy and dilatation are present. The dilatation of the conus arteriosus is much more marked in mitral regurgitation, probably because the left auricular

appendage can easily be displaced dorsad, which affords space for the enlargement of the conus arteriosus, while in the caudal portion of the heart the enlarged left ventricle interferes with the extension of the right ventricle. Left ventricular hypertrophy and dilatation are evidenced by an elongation of the whole heart and by a greater participation of the left ventricle in the formation of the anterior wall of the heart than is the case in pure mitral stenosis. Hence mitral regurgitation provides a transition to the next disease group, in which enlargement of the left ventricle dominates the picture.

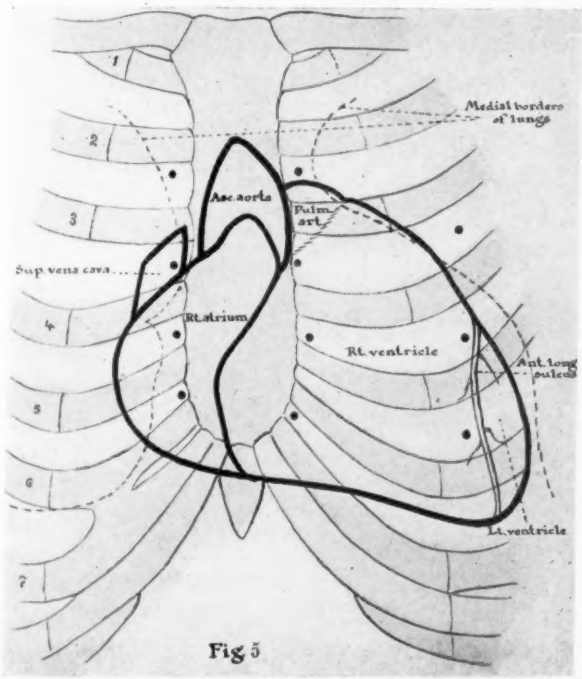

Fig. 5, Case 4.—Pure mitral regurgitation. The right ventricle is dilated to the left and craniad. "Mitral configuration" is very conspicuous. A considerable section of the left ventricle is visible, and the apical portion is somewhat elongated.

B. Heart Diseases in Which Participation of the Left Ventricle Predominates

1. Aortic Regurgitation

Case 5.—Syphilitic aortic regurgitation. The patient was a man, 47 years of age, who weighed 68 kg.; he was above the average in size and was rather heavily built, with a broad thorax.

Autopsy findings (Sept. 8, 1931; No. 126/1931).—The apical portion of the heart was rounded off and was formed by the left ventricle; the left ventricular cavity was moderately large. The greatest thickness of the wall was 2.5 cm. The left atrium was very large; the mitral valve was normal. The right ventricular cavity was dilated; the greatest thickness of the wall was 1.7 cm. The right atrium was dilated, the wall thick. The tricuspid leaflets were normal, as were the pulmonary cusps. The opened pulmonary artery, above the ring, measured 7.5 cm. The

aortic cusps were retracted and thickened at the free edge, particularly the posterior cusp. The aorta, directly above the ring, measured 8.5 cm. From thence the aorta dilated like a sac, particularly toward the right side. The inner surface of the aorta was wrinkled and indurated.

Anterior aspect of the heart (Fig. 6).—The heart was enlarged, particularly in its longitudinal diameter; it appeared cylindrical and elongated to the left and caudad, while its craniocaudal diameter was unchanged. These peculiarities, particularly the rounding of the left lower aspect, indicated enlargement of the left ventricle. This contrasted with the fact that the anterior segment of the left ventricle was scarcely wider than usual. If one compares the surfaces of the two ventricles which are visible on the anterior aspect of the heart, then, as in mitral lesions, the predominance of the right ventricle is unmistakable. In palpating the anterior wall of this heart at autopsy, however, one could prove that the median border of the hypertrophied left ventricle extended actually rather far toward the sternum, about 3 to 4 cm. median to the anterior longitudinal sulcus. The right ventricle, which, on the one hand, was narrowed by the enlarged left ventricle, and, on the other, was subjected to the effect of back stasis from the left side of the heart, made room for itself cephalad; the conus arteriosus extended almost to the second rib, and formed, together with the pulmonary artery and part of the left ventricular contour, a straight oblique line which bridged the "waist of the heart," producing the characteristic "mitralized aortic heart." The right ventricle also extended about 3 cm. beyond the right border of the sternum. Hence only a narrow segment of the right atrium was visible on the anterior aspect of the heart, in spite of the fact that dilatation of that chamber could be demonstrated anatomically. At the same time, the superior vena cava was forced dorsad and could not be seen on the anterior aspect, although the marked dilatation of the ascending aorta might have been partly responsible for this. The aorta extended a considerable distance to both sides of the sternum, particularly to the right. It not only displaced the superior vena cava, but also the pulmonary artery, of which only the smallest segment could be seen anteriorly. In the median line, the lower border of the heart did not extend caudad to the base of the xyphoid process.

The anterior wall of the heart in the presence of left-sided cardiac enlargement.—Enlargement of the left ventricle produces much less easily interpretable conditions than does enlargement of the right ventricle. This is because the bulk of the left ventricle is turned dorsad, and only a relatively small section participates in the formation of the anterior wall of the heart. From the anterior aspect the signs which point to hypertrophy or dilatation of the left ventricle are rather indirect. In general, it can be said that enlargement of the left ventricle proceeds to the left and caudad, while that of the right ventricle extends principally to the left and craniad. Hence the most outstanding sign of left ven-

tricular enlargement is elongation of the whole heart, as shown by a displacement of the apical portion of the heart to the left and caudad. The apical portion appears to be slender and elongated, particularly when tonogenic dilatation (of adaptation) predominates, as in aortic stenosis (see Fig. 7), of which, according to Kirch,[13] the lengthening of the ventricle is characteristic. The subsequent, gradually developing myogenic dilatation (of failure) produces an increasing widening of the ventricle. A more marked bulge of the left border of the heart then becomes visible, and its distance from the midline is increased.

In spite of the shift of the left border of the heart outward, the anterior segment of the left ventricle is usually not appreciably widened. This is because the left ventricle has dilated, not only dorsad, but also considerably to the right and ventrad, thus indenting the median (septal) wall of the right ventricle, whereby a rather large area of contact results between

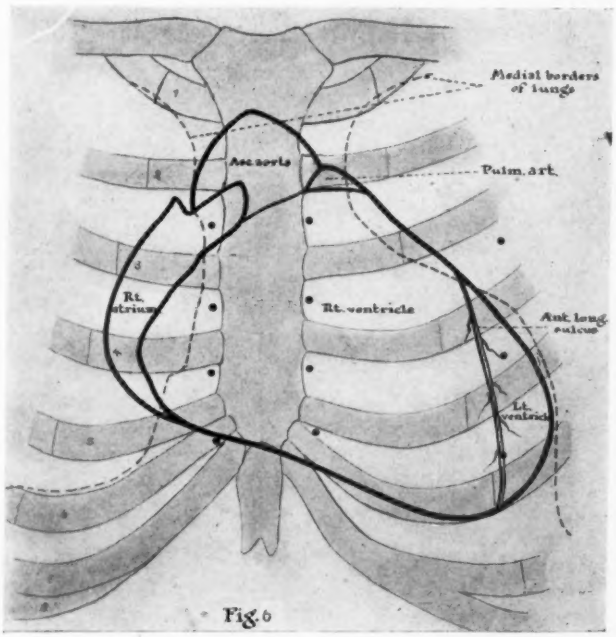

Fig. 6, Case 5.—Syphilitic aortic regurgitation, aneurysmal dilatation of the ascending aorta. The heart is cylindrical and elongated to the left and caudad. The left lower arch bulges. The right ventricle extends considerably to the right of the sternum.

the left median and right anterior ventricular walls. The latter is pulled over to the left, shifting the anterior longitudinal sulcus in the same direction. Thus, the median border of the left ventricle is no longer marked by the anterior longitudinal sulcus but is to be sought several centimeters medial of this line. If one palpates the anterior wall of the right ventricle in such cases, one can feel the true median border of the left ventricle as a line which separates the hypertrophied left ventricle from the thin-walled right ventricle and is rather parallel to, and several

centimeters within, the anterior longitudinal sulcus. Not infrequently this line, particularly if the wall of the right ventricle is not too much thickened, can be actually seen as a shallow longitudinal furrow on the anterior wall of the heart (see Fig. 7). Occasionally the extension of the left ventricle toward the right is so great that the right ventricle is reduced to a narrow, slitlike space (Fig. 7). This phenomenon is known as Bernheim's sign, and has been thought to be responsible for the "mitral failure type" sometimes observed when the heart is the seat of left-sided hypertrophy. The bulging of the septum to the right is apparently caused by enlargement of the outflow tract of the left ventricle, while dilatation of the inflow tract is directed backward, and can be seen fluoroscopically in the left oblique diameter as an extension toward the vertebral column.

The right ventricle, which has been narrowed from the left and dorsad by the bulging left ventricle, must extend in another direction. This is accomplished partly by dilatation of the conus arteriosus (Talma[17]), which bulges to the left and cephalad, displaces the left auricular appendage dorsad, and participates to a greater or less extent in the formation of the left border of the heart. It has been said that the right ventricle, however much it may be encroached upon by the left ventricle, never undergoes a marked distention to the right and never extends far beyond the right sternal border.[17] This, in our experience, is not correct. In many cases of left ventricular enlargement, the right ventricle makes room for itself beyond the right sternal border, which it may pass by several centimeters, provided that it is not hindered in this direction by a marked dilatation of the right atrium. It is natural that this dilatation to the right should be particularly pronounced when considerable stasis is added to the compression caused by the left ventricle. Thus we understand that the right ventricle may occupy the greatest part of the anterior wall of the heart, even when hypertrophy and dilatation of the left ventricle predominate.

Left-sided enlargement of the heart, as a rule, is not associated with an appreciable caudad shift of the lower heart border in the midline. It is the apical portion of the heart which is displaced outward and caudad by the enlargement of the left ventricle. The origin of the aorta may undergo a shift to the right in connection with the median extension of the outflow tract of the left ventricle. The ascending aorta then takes a course which, instead of being vertical, proceeds obliquely from a right caudad to a left cephalad direction, in order to reach the left bronchus. Elongation of the aorta and a high level of the diaphragm may occasionally contribute to this abnormal course. The right atrium, as has been stated, may be displaced dorsad and to the right by the space-seeking right ventricle, so that its lateral border is abnormally distant from the midline and shows increased convexity.

Enlargement of the left atrium occurs primarily dorsad. The view originally promulgated,[11] that dilatation of the left atrium causes the "mitral configuration" of the heart, has been found untenable, as has been indicated above. In some cases, and only with great dilatation, does the left atrium become visible in the right lung field and participate in the formation of the right border of the heart. Unfortunately, I have not had the opportunity to study such a case at autopsy. Only very rarely will pathologic conditions cause the left atrium to appear on the anterior aspect of the heart at all, chiefly because enlargement of the right, as well as of the left, ventricle has the tendency to displace the left auricular appendage entirely out of the visual field. It is not surprising to find that, in the twenty-five cases studied, the left auricular appendage participated in the formation of the anterior wall of the heart only twice, and then by only a small segment, while in the other cases not even a narrow line of the auricular appendage was seen.

2. AORTIC STENOSIS

Uncomplicated aortic stenosis is so rarely met with that if one wishes to study the peculiarities of this valvular lesion it is necessary to use cases of combined valvular lesions in which the aortic stenosis dominates the clinical picture.

CASE 6.—High-grade aortic stenosis, with aoritic regurgitation and mitral stenosis. The patient was a woman, 65 years of age, who weighed 40 kg. She was small and slender and had a long, narrow thorax.

Autopsy findings (March 12, 1931; No. 44/1931).—The heart was moderately enlarged and plump, and was formed for the most part by the left ventricle; the right ventricle was markedly compressed. The apex was rounded and formed by the left ventricle. The left ventricular cavity was not dilated; its wall measured as much as 2.5 cm. in thickness. The mitral ostium scarcely admitted the tip of the little finger. The chordae tendineae of the mitral valves were shortened and thickened. The right ventricular cavity was definitely small; its wall measured as much as 1.2 cm. in thickness. The aortic orifice was very narrow, and the cusps were fused, rigid, and retracted. The ascending aorta measured 7.5 cm. The inner surface of the ascending portion of the aorta was smooth, but in the region of the arch there were confluent calcareous plaques. The ostia of the coronary arteries were wide, and the intima of the arteries was unchanged throughout. The tricuspid and pulmonary valves were normal. The pulmonary artery measured 7.0 cm.

Anterior aspect of the heart (Fig. 7).—The heart was very distinctly enlarged longitudinally; the apical portion, which reached almost to the seventh rib, appeared to be drawn into a sharp, "duck-beak" tip. In contrast, no enlargement of the heart was found in the craniocaudal direction. As a result of the marked lengthening of the heart, the caudal border showed a peculiarly curved contour, and sloped with an increased angle of inclination down toward the left. The contour of the left ventricle was sharply curved, and the border extended almost 2.0 cm. beyond the left midclavicular line, but the segment of the left ventricle which was visible from the front was only slightly widened. The left ventricle bulged sharply to the right into the right ventricular cavity, as was

indicated by a longitudinal furrow, situated almost 4.0 cm. within the anterior longitudinal sulcus, which represented the actual median border of the left ventricle. The right ventricular cavity was greatly narrowed by the septal bulge, so that the pathologist spoke of a "stenosing" of the right ventricle. Actually, nothing in the anterior aspect suggested vicarious dilatation of the right ventricle. The right atrium was moderately dilated; its outer border extended about 3.0 cm. beyond the right sternal line. The area of the wide, heaving, apical thrust which had been palpated in the sixth intercostal space was marked accurately before death; immediately after death a needle was introduced vertically through the chest wall at this point. It met the heart exactly at the apex (Fig. 7*E*).

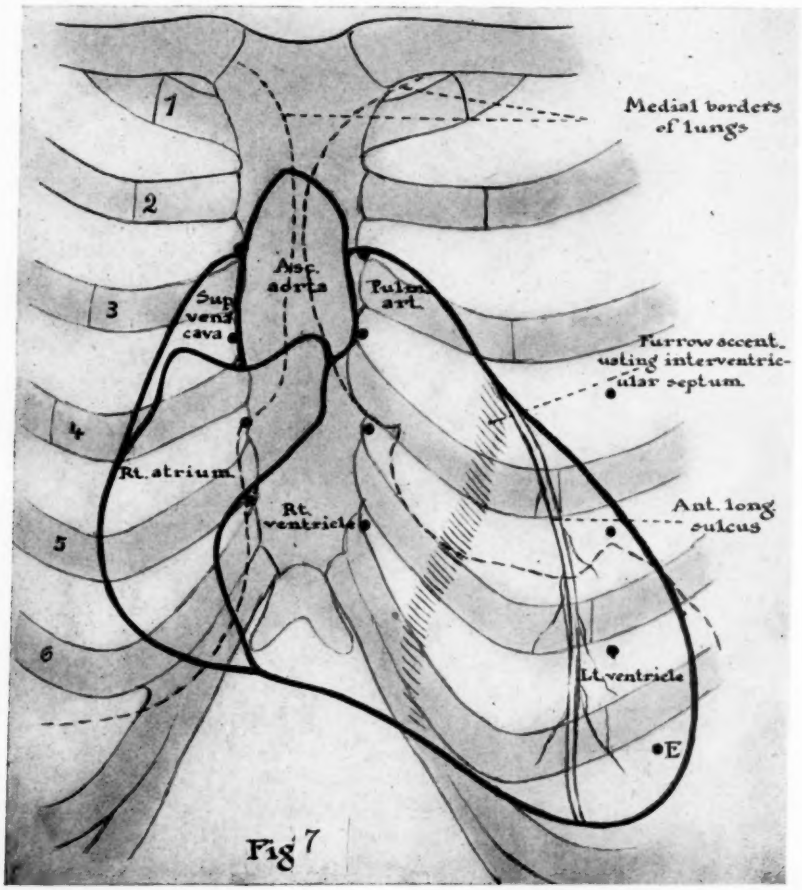

Fig. 7, Case 6.—Marked degree of aortic stenosis (and regurgitation) and mitral stenosis. The heart is distinctly enlarged longitudinally; the apical portion is "duck-beak" like. A furrow inside the anterior longitudinal sulcus marks the actual median border of the enlarged left ventricle. The segment of the right ventricle is rather narrow.

In connection with the marked "stenosing" of the right ventricle by the enlarged left ventricle, it is particularly noteworthy that the pathologist found concentric hypertrophy of the left ventricle in this case.

Kirch[13] described two different forms of ventricular dilatation. With tonogenic (accommodative) dilatation, elongation of the ventricle predominates, whereas with myogenic (failure) dilatation there is a widening of the ventricle. Kirch observed tonogenic dilatation with hypertension and aortic stenosis. Our case of elongation of the heart, in which the apical portion was drawn out into a peculiar, narrow, "duck-beak" shape, appears to be an example of tonogenic dilatation of the left ventricle. The absence of enlargement of the right ventricle, which so often accompanies left-sided enlargement, renders this case particularly fit to illustrate the changes produced by left ventricular hypertrophy.

3. VENTRICULAR ANEURYSM

CASE 7.—Two aneurysms of the left ventricle. The patient was a man, 50 years of age, who weighed 63 kg. He was strongly built, over medium size, and had a broad, deep chest.

Seven weeks prior to death the patient had a severe and prolonged attack of anginal pain. This was followed by continuous gallop rhythm, frequent attacks of pulmonary edema, pronounced pallor of the face, and general restlessness.

Autopsy findings (Oct. 26, 1931; No. 149/1931).—The pericardium was everywhere adherent, less firmly on the anterior surface than posteriorly. The heart was large; the greatest transverse diameter was about 14.0 cm. The apex was round, was formed by the left ventricle, and bulged like a sac. The anterior wall, below the base of the heart, near the left border, projected in the form of a bulge as large as a walnut. The wall of the heart in the region of the sac-like dilatation, near the tip of the left ventricle, was found to be greatly thinned, scarcely 0.3 cm. in thickness, and fibrous. Above the bulge, the wall was 2.0 cm. thick. The mitral leaflets and aortic cusps were normal. The aorta above the ring measured 7.0 cm.; the intima was almost entirely smooth and glistening, showing only occasional fatty-yellow sprinkling. The pulmonary artery above the ring measured 9.0 cm.; the intima was smooth and glistening. The wall of the left coronary artery, immediately beyond the ostium, was greatly calcified, and the lumen greatly narrowed.

Anterior aspect of the heart (Fig. 8).—An unusually broad section of the left ventricle (6.0 cm. in diameter) participated in the formation of the anterior wall of the heart. Yet the heart did not show an increase in the longitudinal diameter, as is usually the case in left ventricular enlargement, but was dilated transversely. This dilatation was caused by a half-spherical bulge of the left border of the heart which corresponded exactly to the large aneurysm in the lower half of the left ventricle. A smaller bulge was seen in the basal portion of the left border of the heart at the point where the pathologist found a second, walnut-sized aneurysm of the wall of the left ventricle. The anterior longitudinal sulcus was displaced somewhat toward the sternum. In addition to the two aneurysms, there was a high degree of eccentric hypertrophy of the left ventricle which narrowed the right ventricle. The latter made room for itself to the right by displacing the right atrium dorsad, and even extended 4 cm. beyond the right border of the sternum. Hence only a narrow segment of the right atrium could be seen from the anterior aspect; the left auricular appendage was again

displaced entirely out of sight. There was little enlargement of the heart in the craniocaudal direction.

The type of enlargement and configuration described here appears to be characteristic of aneurysm of the ventricle—if I may be allowed to draw conclusions from this and from another similar case which I observed. In both cases the left border of the heart bulged greatly, and the anterior segment of the left ventricle appeared to be much increased in size. This was in contrast to the cases of hypertrophy of the left side of the heart, in which enlargement in the longitudinal diameter was the most striking finding, while the anterior section of the left ventricle was not particularly increased in area (See Figs. 6 and 7). Hence, in aneurysm of the ventricle, the heart is found to be enlarged transversely, with an unusually large portion of the left ventricle sharing the anterior aspect of the heart. The left border may show deformities, such as a circumscribed bulge or a hump, which, as a rule, are less distinct than those observed in the roentgenogram.

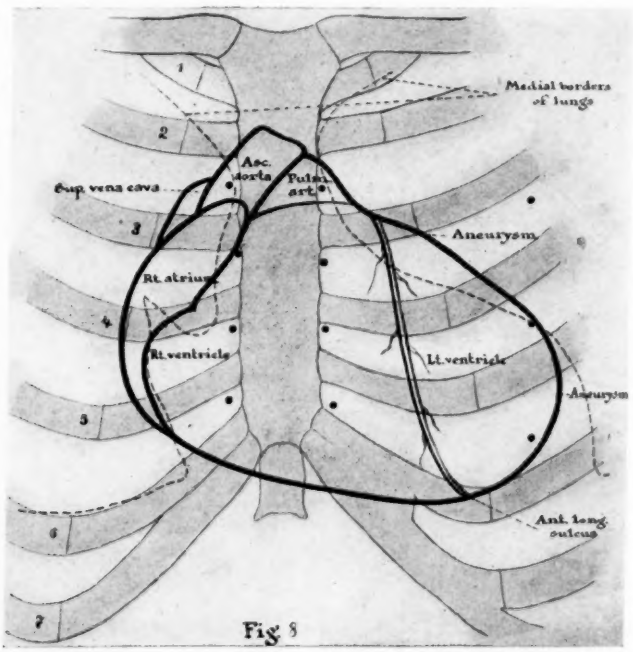

Fig. 8, Case 7.—Two aneurysms of the anterior and lateral wall of the left ventricle, the smaller basal, the greater near the apical region. Note the large section of the left ventricle visible from the front and its bulging lateral outline. The right ventricle extends considerably beyond the right margin of the sternum.

POST-MORTEM CHANGES. RESULTS OF ANATOMIC AND ROENTGENOLOGIC STUDIES

When we review the results of our examinations, the following question naturally arises: to what extent can the anatomic drawings be correlated with conditions during life? We know that, after death, vari-

ous intracardiac and extracardiac factors work together to change the size, shape, and position of the heart. Among the extracardiac factors are (1) diminution of the elastic pull of the lungs on the pericardium and also on the heart at the moment when the thorax is opened; (2) high position of the diaphragm resulting from post-mortem decrease in tonus. Roentgenologic examinations have shown how decisively the shape of the heart is influenced by the position of the diaphragm. Intracardiac factors to be considered are: (1) The decrease in the tonus of the myocardium which occurs during agony;[18] as a result of the relaxation of the myocardium, there is a dilatation of the heart (primary dilatation of Rothberger[19]). (2) Processes during rigor mortis which change the filling of the various cavities of the heart (Rothberger,[19] Volkhardt[4]). At the onset of rigor mortis, which begins at the earliest within a half-hour after death and, as a rule, disappears after twenty-four hours, the left ventricle contracts and forces most of its blood into the empty arteries, whereas the right ventricle, whose muscle is not so strong, is not able to expel a considerable amount of blood into the pulmonary vessels which became engorged during agony. Hence, the right ventricle remains filled with blood during the period of rigor mortis, while the volume of the left ventricle is greatly diminished. When rigor mortis ceases, the latter relaxes, yet it contains little or no blood, for the contents of the aorta and the left atrium have coagulated in the meantime, and cannot flow into the left ventricle. The right ventricle, on the contrary, retains its engorgement almost unchanged.

All these facts relate primarily to the normal heart. Volkhardt, from the Pathologic Institute of Aschoff, in Freiburg, has stated this expressly, and has stressed that in heart disease the processes of rigor mortis are scarcely able to obscure or to affect the changes in shape which were present during life. The dilated left ventricle will, for instance, remain filled with blood at the height of rigor mortis. Further, it has been stated[19] that the degree of rigor mortis of the heart is less if the myocardium has degenerated, and that it may be lacking entirely. There can be no doubt that we have had to do with high-grade degeneration of the myocardium in the cases considered in the present discussion. Finally, we must remember that even though death always occurs during diastole, the myocardium retains a certain amount of tonus for some time after death, and is capable of tonic contraction.[19] It is known that the irritability of the myocardium can persist for a considerable period after death. Thus, heart movements were observed in the cadaver twenty-nine hours after the death of a woman who was executed.

From all this, one may conclude that conditions after death, particularly in pathologically changed hearts, do not deviate so greatly from those during life, and that one may utilize observations on the former to explain the latter. We are thus in agreement with Assmann,[9] who stressed that one should not overemphasize the post-mortem changes in

the heart. Undoubtedly, the high position assumed by the diaphragm after death influences the shape of the heart, so that roentgenograms, which are usually made with patients in the upright position, cannot be compared directly with drawings of the anterior wall of the heart made from the cadaver. Keeping in mind the differences caused by the changed position of the diaphragm, there was, in the majority of our anatomically examined cases, a satisfactory agreement between the roentgenogram and the anatomic drawing, both as to size and shape of the heart. Roentgenologic examination naturally has a great advantage, for it enables one to examine the living heart, and to follow the various stages in the development of pathologic processes, whereas the depiction of the heart of the cadaver shows only the end result. Undoubtedly, the roentgenologic examination, under all conditions, deserves preference if we want to obtain information concerning what form and shape of the heart are characteristic of a definite pathologic condition. But fluoroscopy gives us, as was stated earlier, only a silhouette, the equivalent of an empty frame. To fill this frame with a visible picture was the purpose of these anatomic examinations.

SUMMARY

This is a report of anatomic examinations which sought to ascertain the configuration and structure of the anterior wall of the heart and its topographic relationships to the anterior chest wall under various pathologic conditions. To this end, the anterior wall of the heart was delineated in natural size and position in the cadavers of twenty-five cardiac patients. The use of a special method made it possible to relate the spatial relations of the anterior wall of the heart to the anterior wall of the chest.

Diagrams obtained in this manner, because of their details, are a desirable adjuvant to the silhouettes obtained in the living by means of roentgenologic examinations. They substantiate and enlarge the knowledge, obtained by roentgenologic observation, of the growth tendencies of the various parts of the heart in hypertrophy and dilatation, and the resulting changes in the configuration of the anterior wall of the heart. Finally, they give a clear picture of the positional relations of the heart and its components to the anterior chest wall.

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THE ELECTROCARDIOGRAM IN PULMONARY EMBOLISM*

MAURICE SOKOLOW, M.D.,† LOUIS N. KATZ, M.D., AND
ALFRED N. MUSCOVITZ, M.D.
CHICAGO, ILL.

IT HAS been suggested recently that the electrocardiogram may help to differentiate pulmonary embolism from other acute conditions, such as coronary occlusion, with which it may be confused clinically. It is now generally established that the classical triad of severe pain, hemoptysis, and friction rub is often absent in pulmonary embolism, and in such instances other diagnostic aids are necessary. Impetus to the use of the electrocardiogram in this connection was given by McGinn and White,[1] who described a characteristic electrocardiographic contour in pulmonary embolism, namely, the appearance of a prominent S_1 and Q_3, a depression of S-T_1 and S-T_2, with staircase ascent, and an inversion of T_3, with upward bowing of S-T_3. This characteristic curve has also been reported in an occasional case by Barnes,[2] Scherf and Schonbrunner,[3] and Langendorf and Pick.[4] However, Love, et al.,[5] found that this type of electrocardiogram was the exception in their series. The more common changes were nonspecific, consisting of a depression of S-T_1 and S-T_2, with an inverted coronary T_3 and an inverted T in the chest lead; and in five of their twelve cases they found no significant electrocardiographic abnormalities. Langendorf and Pick[4] also noted an electrocardiogram of normal appearance in a number of their patients. Recently, Durant, et al.,[6] found a transient S type of intraventricular block in three cases within the first twenty-four hours of the attack. In view of the differences in previous series, we felt that it was desirable to reinvestigate the subject in a larger series of cases, selected from the hospital files, and to ascertain in these the frequency of the various types of electrocardiographic abnormalities.

SELECTION OF CASES

Fifty cases were found in the hospital records, from 1931 to 1939, in which one or more electrocardiograms had been taken shortly after an acute episode diagnosed as pulmonary embolism had occurred. In twenty-seven patients there was autopsy proof of the diagnosis, and in the other twenty-three, who survived or on whom an autopsy was not performed, the diagnosis was based on the presence of several of the following:

1. A condition known to be able to give rise to pulmonary emboli, e.g., chronic cardiac disease, auricular fibrillation, coronary occlusion, venous thrombosis, the postoperative state, and fracture.

From the Cardiovascular and Pathology Departments, Michael Reese Hospital, Chicago, Ill.

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†Now in San Francisco.

2. An acute attack, characterized by sudden collapse, acute tachypnea and dyspnea, cyanosis, or pleuritic chest pain.

3. A pleural friction rub, hemoptysis, signs of localized pulmonary congestion—often delayed for twenty-four hours.

4. Roentgenologic evidence of the typical triangular shadow or the atypical peripheral shadow suggestive of pulmonary infarction.

5. Aggravation or appearance of cardiac failure or jaundice in a patient with chronic heart disease following such an acute attack.

6. Recurrence of the acute symptoms and signs.

In only two cases were there large riding emboli at autopsy (Fig. 1); the other patients had emboli in the smaller vessels. Sixteen of the patients had electrocardiograms within twelve hours of the attack; fourteen, within the second twelve hours; ten, on the second or third day; and ten, between the third and tenth days. Thirty-four patients had chest Lead CF_2 of the American Heart Association Report, and twelve had CF_4, as well. In three cases the pulmonary embolism occurred after a recent coronary occlusion, and in three cases after an old one. In sixteen cases chronic organic heart disease was present. In seventeen cases an elec-

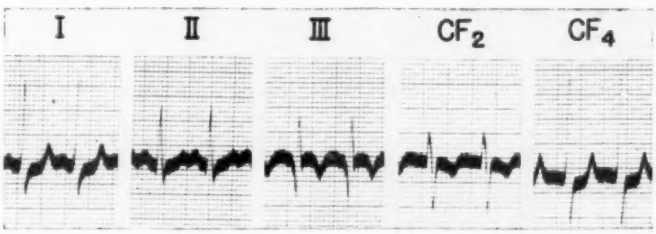

Fig. 1.—Pulmonary embolus shown at autopsy to be a riding embolus which had not produced infarction. Patient 40 years old. Hysterectomy Oct. 21; embolism Oct. 31, record twelve hours later; death, Nov. 1, 1938.

TABLE I

DISTRIBUTION OF ELECTROCARDIOGRAMS IN THIS STUDY

DIAGNOSIS	CASES OF PULMONARY EMBOLISM PROVED AT AUTOPSY	CASES OF PULMONARY EMBOLISM DIAGNOSED CLINICALLY	TOTAL CASES
Group 1	5	4	9
Group 2	16	11	27
Group 3	4	5	9
Group 4	2	3	5
	27	23	50

Group 1. Those which were normal or did not deviate significantly from the control tracing.

Group 2. Those showing nonspecific abnormalities, significant deviation from the control tracing, disturbances of impulse origin or impulse conduction.

Group 3. Those in which there were some of the characteristics of recent myocardial infarction.

Group 4. Those showing the features described by McGinn and White.[1]

trocardiogram was obtained before the acute attack or several months afterward, and these were used as controls in estimating the effect of pulmonary embolism.

CLASSIFICATION OF THE ELECTROCARDIOGRAPHIC CHANGES

Analysis of the data in the fifty cases indicated that the electrocardiographic changes were not uniform. For purposes of differentiation they

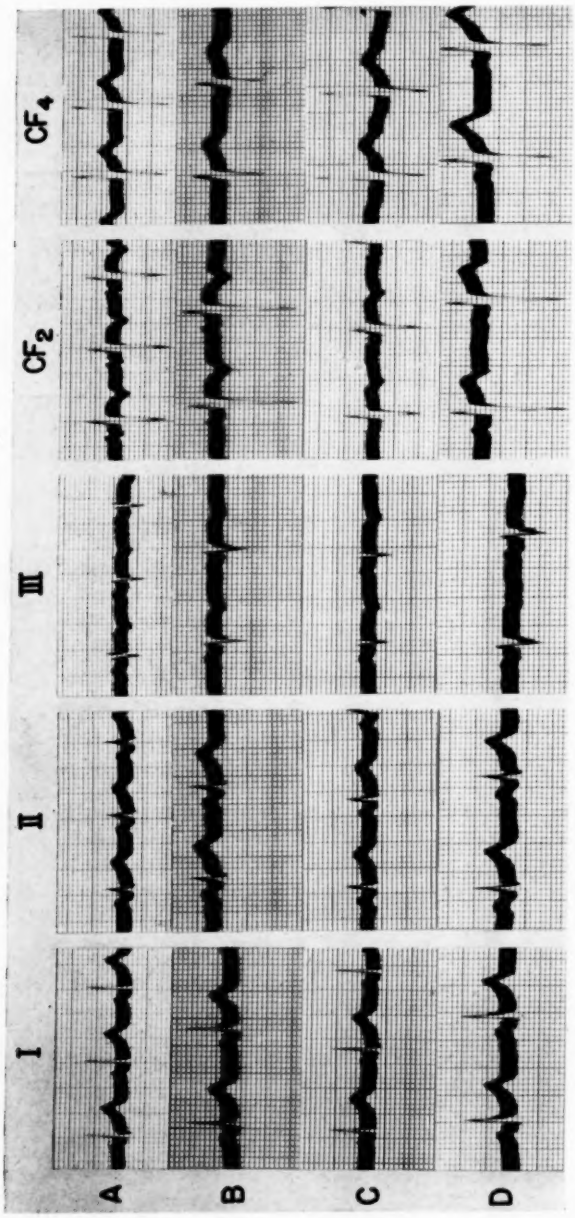

Fig. 2.—A series of pulmonary emboli. Patient 51 years old. Cholecystectomy, Jan. 24; first pulmonary embolus, Feb. 1; second, Feb. 19; third, Feb. 23, 1939. *A*, twenty-four hours, and *B*, five days, after the first, and *C*, twelve hours, and *D*, two months, after the second embolus. Patient survived.

were grouped into four types, as outlined in Table I. It will be seen that the largest group is that in which the nonspecific abnormalities occurred.

In cases in which the diagnosis was proved, no correlation could be made between the degree or type of electrocardiographic abnormality and the number or size of the infarcts. It could not be established whether a difference existed between the electrocardiographic appearance following embolism with, and embolism without, pulmonary infarction, because the former group of cases was disproportionately large, and because the presence of infarction could not always be ascertained with certainty in the patients who did not come to autopsy. However, a large embolus, without infarction, can cause significant electrocardiographic abnormalities (Fig. 1).

The interval which elapsed between the occurrence of the embolism and the recording of the electrocardiogram did not appear to determine the type of change, provided the record was made within the first few days

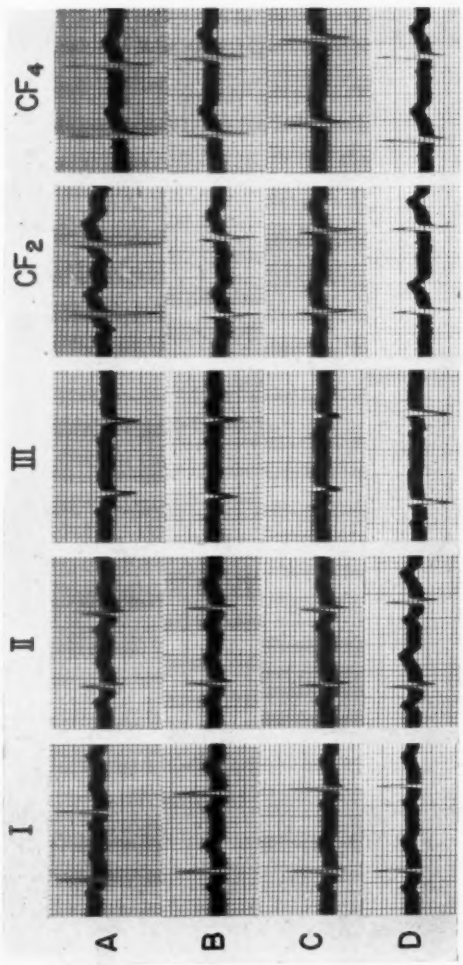

Fig. 3.—Patient 45 years old. Vaginal hysterectomy Feb. 9, 1939; pulmonary embolism, March 31, 1939. *A*, thirteen hours, *B*, three, *C*, seven, and *D*, twelve, days afterwards. Patient survived.

(Table II). It was noted that abnormalities may persist for days, without much alteration (Fig. 2). However, in some cases it was found that transitory changes were present which would have been missed if the electrocardiogram had been taken later (Fig. 3).

GROUP I

Tracings which were essentially normal, or not significantly different from control tracings

Nine of the fifty cases were placed in this group. This incidence is probably too low, because in some of the cases in which there was a single abnormal tracing the abnormality may have been present before the embolism occurred (Fig. 4). Electrocardiographic abnormalities (Fig. 5*A*) or deviations from control tracings (Fig. 4) did not occur despite the presence of large emboli and moderately large areas of infarction, even when the electrocardiogram was taken within a few days after lodgment of the embolus. In one instance the electrocardiogram was normal within six hours of the acute attack; in five cases the records were normal or unchanged within the first twenty-four hours after embolism occurred (Table II), and in two of these the diagnosis was proved at autopsy.

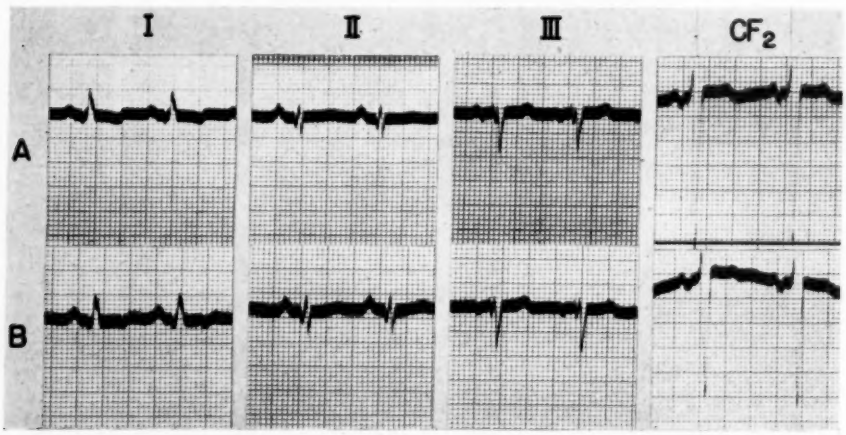

Fig. 4.—Pulmonary emboli proved at autopsy by the presence of multiple pulmonary infarcts. Patient 43 years old. *A*, Oct. 20, 1932; pulmonary embolism, Oct. 23; *B*, Oct. 25; death, Oct. 31, 1932.

GROUP II

Tracings showing nonspecific abnormalities, arrhythmias, or significant deviations from the control tracings

This was the largest group, comprising twenty-seven out of fifty cases. No attempt was made to estimate the frequency of occurrence of each variation from normal, particularly because, in many of the cases, there were no control electrocardiograms, and the abnormalities present may have antedated the embolism (Fig. 4).

TABLE II

RELATION OF CONTOUR OF ELECTROCARDIOGRAM TO TIME AFTER ACUTE ATTACK AT WHICH RECORD WAS TAKEN

	GROUP 1*			GROUP 2			GROUP 3			GROUP 4			
RECORD TAKEN	AUTOPSY CASES	CLINICAL DIAGNOSES ONLY	ALL CASES	AUTOPSY CASES	CLINICAL DIAGNOSES ONLY	ALL CASES	AUTOPSY CASES	CLINICAL DIAGNOSES ONLY	ALL CASES	AUTOPSY CASES	CLINICAL DIAGNOSES ONLY	ALL CASES	TOTAL CASES
In first 6 hr.	0	1	1	5	0	5	0	2	2	0	1	1	9
between 7 and 12 hr.	0	1	1	3	2	5	0	0	0	1	0	1	7
between 13 and 24 hr.	2	1	3	4	5	9	1	0	1	0	1	1	14
between second and third day	2	0	2	1	3	4	1	2	3	1	0	1	10
between fourth and seventh day	1	0	1	2	0	2	2	1	3	0	1	1	7
between eighth and tenth day	0	1	1	1	1	2	0	0	0	0	0	0	3

*See Table I for classification of groups.

An analysis was made of the most frequent changes in the seventeen cases of all groups in which there were control records, merely to indicate the trend. The most frequent transitory changes were (1) slight to moderate depression of S-T_1 and S-T_2 (Fig. 6), (2) decrease in the voltage of the QRS complexes in Leads I and II (Figs. 6 and 9), (3) inversion of T_3, occasionally with the coronary contour (Fig. 1), (4)

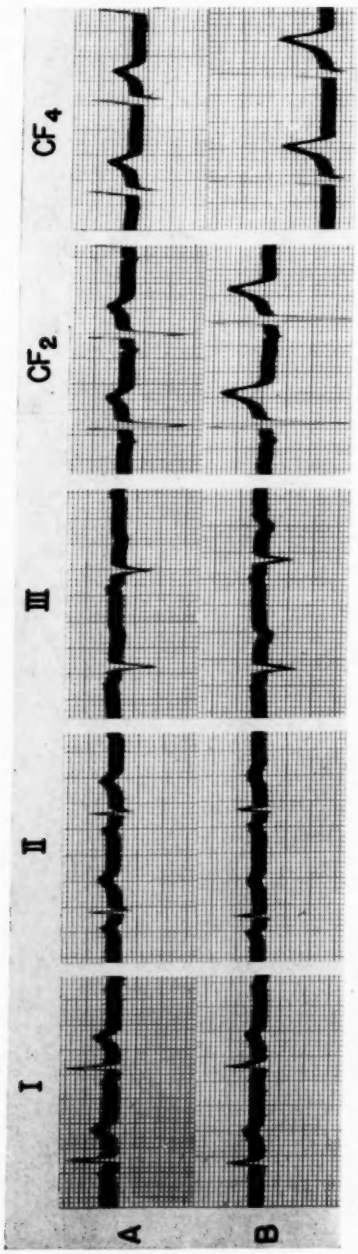

Fig. 5.—A series of pulmonary emboli. Patient 57 years old. Acute thrombophlebitis of left leg, Nov. 29; left saphenous ligation, Dec. 3; pulmonary emboli, Dec. 9, Dec. 11, Dec. 13, 1938. *A*, eight hours, and *B*, four days, after the third embolus. Patient survived.

change in the size of the T wave in one or more leads (Figs. 2, 3, 6, 8), (5) right axis deviation (Fig. 10), (6) appearance of a Q_3 or S_1 (Figs. 6, 8, 9, 10), (7) slight elevation of S-T in CF_2 (Fig. 3), (8) definite inversion of T in CF_2 (Figs. 2 and 8), and (9) various arrhythmias (Figs. 7 and 11). These individual changes occurred alone in some instances, but more often in various combinations, as inspection of the above curves will show.

Transitory right axis deviation was noted in a number of instances, and occasionally was striking (Fig. 10). In no instance did left axis deviation develop after the occurrence of embolism. In all instances in which there were control records and left axis deviation was found, it was present before the acute attack (Figs. 2, 3, 4, 7, 9). In Fig. 8*B*, the presence of a large Q_3 simulated left axis deviation. Our analysis shows that the appearance of a large S_1 and a deviation of the axis to the right occurred in the majority of the cases in which there were control records. In accord with McGinn and White,[1] we consider such an unexpected right axis deviation following an acute attack as an important finding. The only other acute condition which leads to right axis deviation is anterior infarction of the heart,[8] but here a Q_1, rather than an S_1, appears. Since the electrocardiogram in pulmonary embolism is rarely confused with that in anterior infarction, right axis deviation is an important diagnostic aid in pulmonary embolism. The appearance of left axis deviation after an acute attack militates against the possibility of pulmonary embolism; it did not occur in our series.

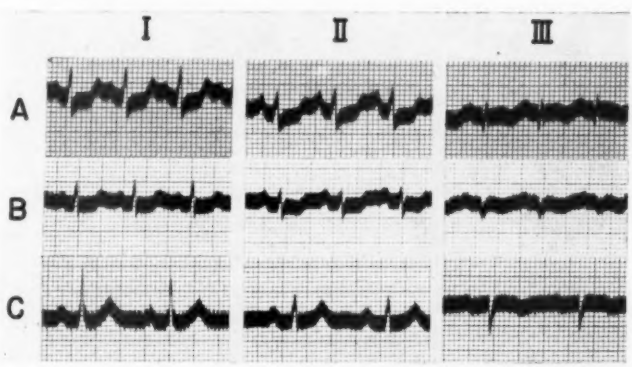

Fig. 6.—A series of pulmonary emboli. Patient 46 years old. Appendectomy, Jan. 5, 1932; two minor pulmonary emboli, Jan. 16 and Feb. 10 and a third major pulmonary embolus, Feb. 13, 1932; *A*, five hours, *B*, six days and *C*, a month after the third embolus. Patient survived.

Ectopic rhythms and conduction defects of all types were frequently noted; eighteen of the fifty patients showed such abnormalities. Of the seventeen patients who had control records, three developed ectopic rhythms. In a number of cases, a cardiac irregularity was noted clinically after the embolus had lodged, but no electrocardiograms were obtained to confirm this observation. Occasionally, the ectopic rhythm was

very bizarre and "prefibrillatory" in character (Fig. 11). These disturbances could not be ascribed to digitalis, for most of these patients had not received this drug. Auriculoventricular and intraventricular block, and, in one instance, S-A block not attributable to digitalis, were seen in tracings after the occurrence of pulmonary emboli, but, unfortunately, in none of these cases was there a control record to rule out the possibility that the condition had antedated the embolism.

GROUP III

Tracings showing some of the characteristics of recent myocardial infarction

If we exclude the five cases of the McGinn-White type, the electrocardiograms of nine patients fell into this group. The resemblance to

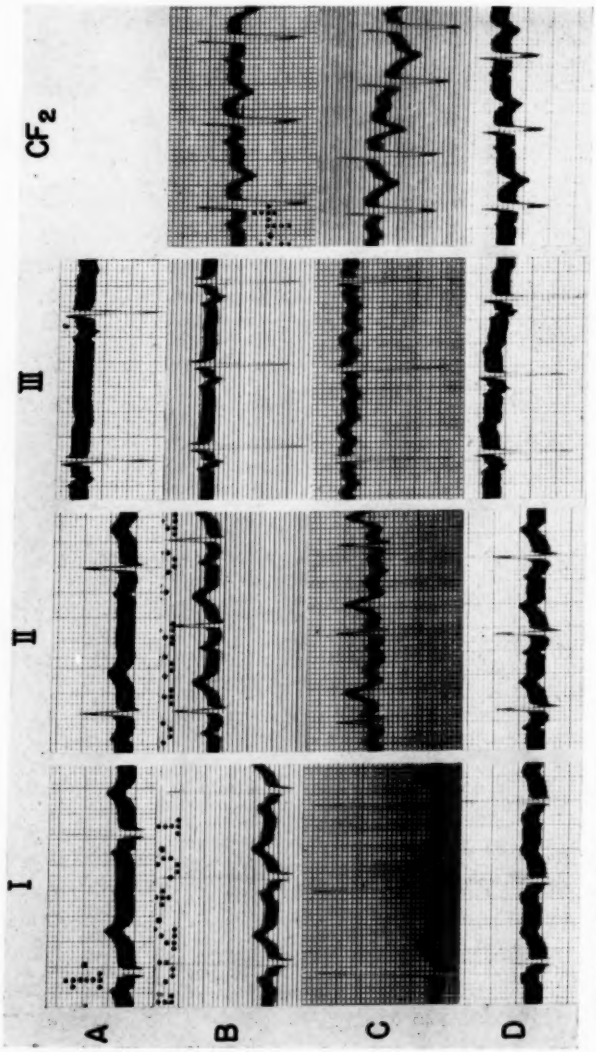

Fig. 7.—Pulmonary emboli proved at autopsy by the presence of multiple, bilateral pulmonary emboli and infarcts of various ages. Patient 68 years old. *A*, Nov. 25; suprapubic cystotomy, Nov. 26; pulmonary emboli, Nov. 30 and Dec. 8; *B*, *C*, and *D*, Dec. 8, Dec. 10, and Dec. 27; third pulmonary embolus, Dec. 28. Death suddenly, Dec. 30, 1935.

coronary occlusion was often superficial, but when there has been an acute attack simulating coronary occlusion, even such changes may lead to an electrocardiographic diagnosis of coronary occlusion, particularly because atypical changes are not infrequently seen in cases of recent coronary occlusion in which the diagnosis is proved.[8]

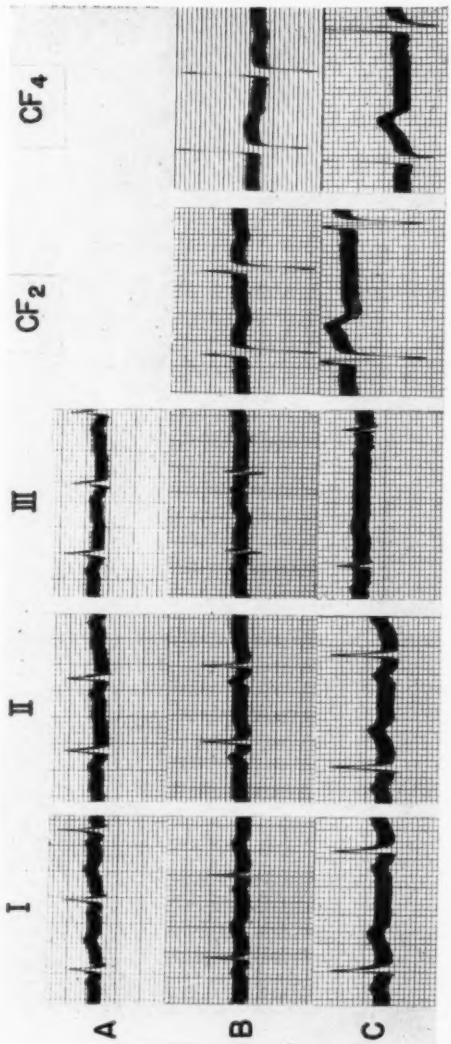

Fig. 8.—Patient 45 years old. Bowel resection, Nov. 16; pulmonary embolus, Nov. 26, 1938. *A*, six hours, *B*, four days, and *C*, four and one-half months, afterwards. Patient survived.

Anterior myocardial infarction was simulated in chest Lead CF_2 by the slight elevation of S-T, occasionally with an upward convexity (Fig. 2), and especially by definite inversion of T. However, QRS in this lead retained its normal diphasic appearance (Figs. 1, 2, 7, and 8). The differentiation was rarely difficult because of the appearance of QRS in this chest lead and its contour in the limb leads. In only one case was the diagnosis seriously in doubt.

Posterior infarction, however, was more often simulated in the limb leads, and, on two occasions, also in the chest leads. Characteristically, this type of myocardial infarction produces depression of S-T_1 and S-T in CF_2 and elevation of S-T_2 and S-T_3, with a prominent Q_3 and an inverted T_2 and T_3. In cases of pulmonary embolism there are rarely a depression of S-T in CF_2, inversion of T_2, and elevation of S-T_2, except when the embolus occurs after myocardial infarction (Fig. 12). Further, right axis deviation is rare after posterior infarction (Bohning and Katz[8]). Langendorf and Pick[4] noted that Lead II resembles Lead III after posterior infarction, but is more like Lead I after pulmonary embolism (see also Figs. 1 and 6). Occasionally, the only abnormality in the limb leads is the presence of a prominent Q_3, an elevated, bowed-up S-T_3 inversion of T_3 (Figs. 2 and 8). These changes are distinguished from those caused by posterior infarction by the absence of the other electrocardiographic signs of myocardial infarction, and by the rapid return to normal. In these cases the Q_3 may disappear, leaving only an inverted T_3, and this is not usual in myocardial infarction. Confusion with the type of curve described by Wood, Wolferth, and Bellet[9]

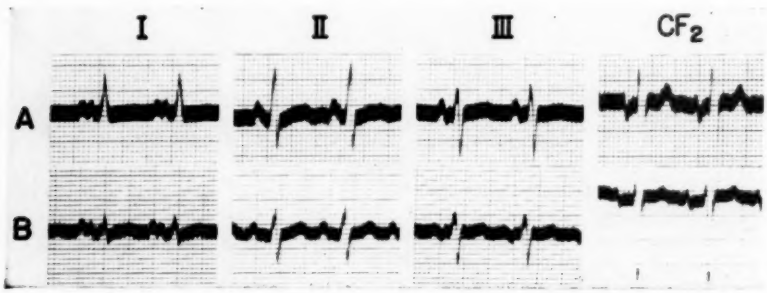

Fig. 9.—Pulmonary emboli proved at autopsy by the presence of multiple pulmonary infarcts of various ages. Patient 36 years old, with chronic rheumatic heart disease. Minor pulmonary embolic attacks, Aug. 3 and Aug. 29, 1937. *A*, Aug. 31; major pulmonary embolus, Sept. 11; *B*, four hours later; death, Sept. 15, 1937.

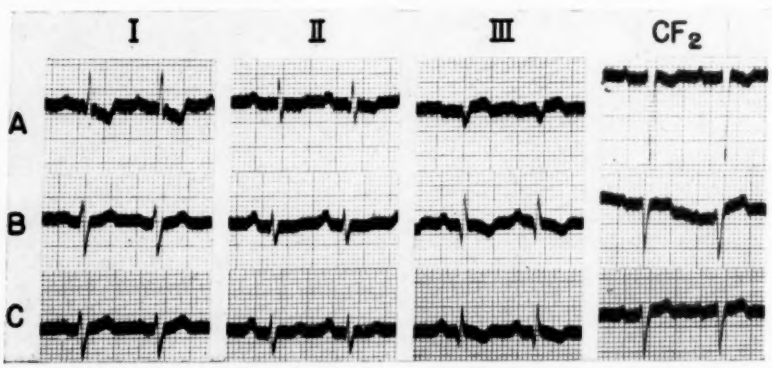

Fig. 10.—A series of pulmonary emboli. Patient 47 years old with rheumatic heart disease and aortic valve incompetence. Venous thrombosis of right leg, June 29; *A*, July 2; pulmonary emboli, Aug. 9, and Aug. 17; *B*, twelve hours later; *C*, Aug. 20; third pulmonary embolus Aug. 21; death, one hour later. No autopsy.

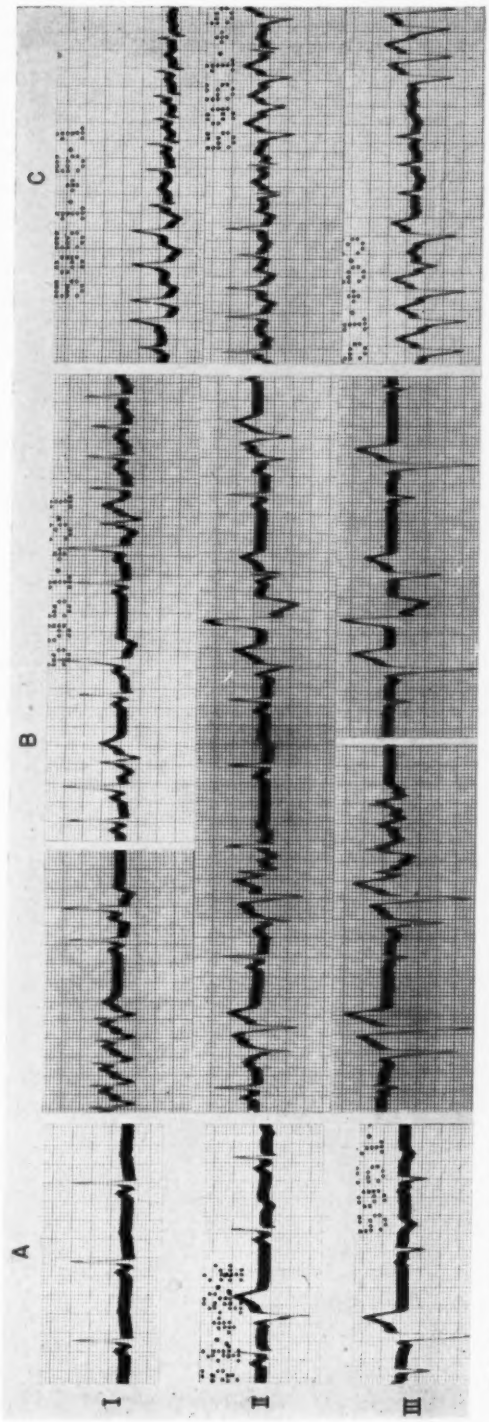

Fig. 11.—Pulmonary emboli proved at autopsy by the presence of multiple pulmonary infarcts of various ages, one of which was old and contained a necrotic cavity. Patient 60 years old. *A*, Dec. 15; suprapubic cystotomy, Dec. 16; first pulmonary embolus, Dec. 18; *B*, fifteen hours later; second and third pulmonary emboli, Dec. 23, 1932 and Jan. 6, 1933; *C*, a few hours after last embolus; fourth pulmonary embolus, Jan. 9: death, Jan. 24, 1933.

as characteristic of lateral wall infarction (viz., depressed $S\text{-}T_1$, $S\text{-}T_2$, and S-T in CF_4) occurred in two cases. A more frequent combination which resembles atypical signs of myocardial infarction, not sufficiently stressed heretofore, is the occurrence in the limb leads of changes suggesting posterior infarction, and, in the chest leads, of changes suggesting anterior infarction (Figs. 2, 7, and 8).

GROUP IV

Tracings of the McGinn and White type

This kind of change was seen in five of the fifty cases. This characteristic type of electrocardiogram is, therefore, infrequent, although its various individual components are noted more often. The individual changes, however, are not diagnostically significant, and cases in which they occurred were placed in the nonspecific group. As will be seen in Table II, the records from patients with this type of electrocardiogram were taken from six hours to six days after the embolism occurred. Illustrative cases are shown in Figs. 1 and 6.

THE OCCURRENCE OF PULMONARY EMBOLISM IN PATIENTS WHO HAD PREVIOUSLY HAD MYOCARDIAL INFARCTION

In patients who have previously had myocardial infarction, a pulmonary embolus may give rise to changes resembling those which occurred in the early stages of the infarction, making the differential diagnosis impossible when only limb leads are taken (Fig. 12).

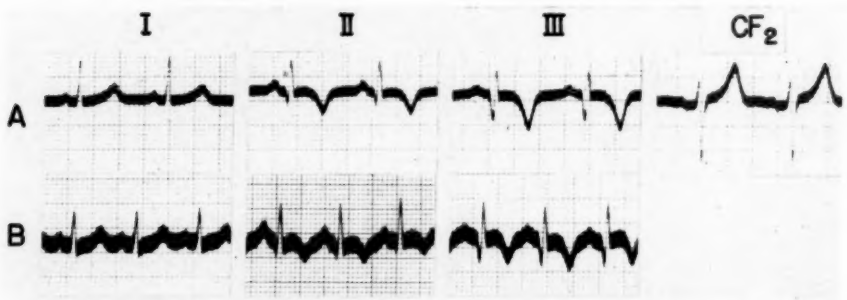

Fig. 12.—Pulmonary embolus proved at autopsy by the presence of multiple infarctions in the middle and lower lobes of the right lung. Patient 64 years old. The posterior myocardial infarct which occurred three months before death was also demonstrated at autopsy. Coronary occlusion July 1, 1933; *A*, last of a series of curves, Sept. 14, 1933; pulmonary embolus Sept. 26; *B*, Sept. 27; death, Oct. 1, 1933.

Coronary occlusion is often followed by a second acute attack within the first fortnight. The question then arises whether a second infarction or a pulmonary embolism has occurred (Fig. 13). When the classical signs, i.e., hemoptysis and pleural friction rub, do not appear, the diagnosis is difficult (Hamburger and Saphir[7]). In this series we have included several cases (diagnosis proved at autopsy) in which a pulmonary

embolus occurred soon after coronary occlusion (Fig. 13). In two other instances, no further changes were noted; in one, auricular flutter occurred, but in this case the pulmonary embolus followed so closely upon the coronary occlusion that the flutter may have been caused by the latter.

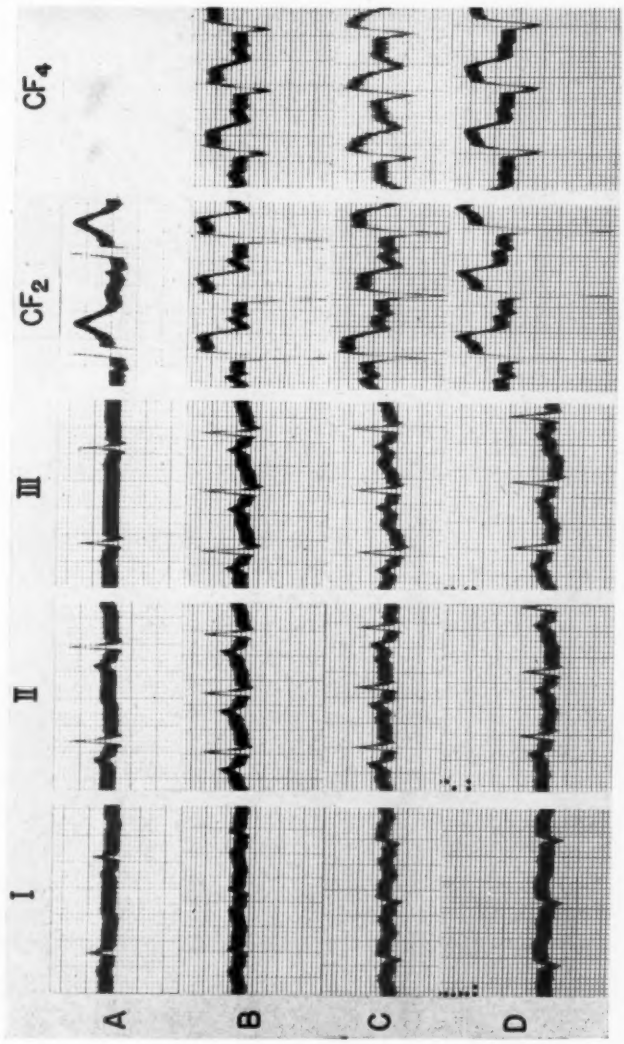

Fig. 13.—Pulmonary embolus proved at autopsy by the presence of an embolus, with infarction of the upper lobe of the right lung. Patient 58 years old. The old posterior and recent anterior myocardial infarcts were also demonstrated at autopsy. Posterior myocardial infarction Oct. 1, 1937; *A*, same day; anterior myocardial infarction July 14, 1938; *B*, same day; pulmonary embolus, July 15; *C* and *D*, July 16 and July 25; death, Aug. 3, 1938.

IMPORTANCE OF SERIAL CURVES

The evolution of the electrocardiographic changes in myocardial infarction is often characteristic, and, in many cases in which the initial changes are not striking, subsequently developing abnormalities make the diagnosis certain. It has been stated that these typical evolutionary changes do not occur in pulmonary embolism (Master, Jaffe, and Dack,[10]

Langendorf and Pick[4]), but, to our knowledge, the only extensive serial curves which have been published are those of Durant, et al.[6] They did not describe any subsequent, characteristic changes in the T wave. We had the opportunity of studying serial curves in seventeen of our cases, and typical ones are illustrated in Figs. 2, 3, 5-10.

In these cases it is seen that no characteristic evolutionary changes occurred. Often the changes are transient, and, in the case of the S-T depression, may disappear in a few days (Fig. 3). No T-wave evolution occurred, and, unlike in myocardial infarction, the major T-wave changes were found in the first tracing taken after the attack. The return to normal required a variable amount of time, but was almost always without any particular evolutionary pattern. In an occasional case (Fig. 8) there may be a delay in the appearance of the large Q_3. The maximum S-T depression, which usually occurs early, on rare occasions is delayed. The failure of characteristic evolutionary changes to appear, therefore, favors the diagnosis of pulmonary embolism. Occasionally, in serial curves, all of which were normal, the contour was found to vary from time to time (Fig. 5); at other times the transient abnormalities were confined to Lead III and chest Lead CF_2 (Fig. 2).

Occasionally, the differential diagnosis between coronary occlusion and pulmonary embolism is impossible, even with serial curves (Fig. 14). This study has emphasized the greater utility of CF_2 over CF_4 (and presumably, therefore, also over IVF) in differentiating between pulmonary embolism and myocardial infarction.

THE ELECTROCARDIOGRAPHIC DIAGNOSIS OF PULMONARY EMBOLISM

In our series, no consistently characteristic electrocardiographic abnormality was found in pulmonary embolism. Normal or nonspecific abnormalities of no diagnostic value occurred in about half of the cases. The absence of significant electrocardiographic changes, however, when an acute attack makes it necessary to differentiate between pulmonary embolism and coronary occlusion, may help in a negative way, although such changes may also be absent in the first few days in occasional cases of myocardial infarction (Sampson and Eliaser,[11] Feil[12]). The frequency with which certain aberrations appear (depressed $S\text{-}T_1$ and $S\text{-}T_2$, low "voltage", Q_3, inversion of T_3, right axis deviation, inversion of T in CF_2) and the rarity of others (elevation of $S\text{-}T_1$ or $S\text{-}T_2$, inversion of T_2, depression of S-T in CF_2, characteristic evolution) are positive aids in making the diagnosis. In the final analysis, the most important diagnostic procedure is a careful correlation between the clinical manifestations and the electrocardiograms. Atypical changes suggestive of recent myocardial infarction should arouse the suspicion of the possibility of pulmonary embolism, and the patient should be investigated with this in mind. The appearance of a pleural friction rub, hemoptysis, jaundice, marked cardiac failure, roentgenologic evidence of pulmonary infarction, or the discovery of a venous thrombosis, makes the diagnosis of pulmo-

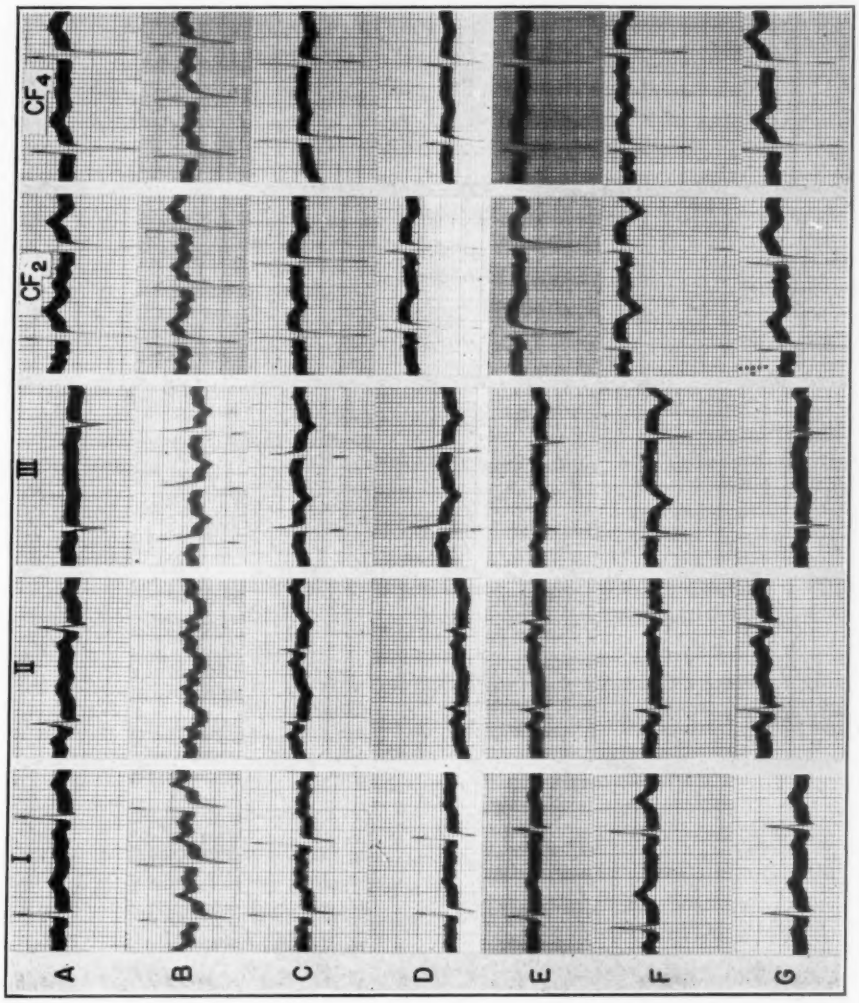

Fig. 14.—An acute attack caused either by pulmonary embolism or coronary occlusion. Patient, 54 years old, had diabetes mellitus. *A*, Feb. 10; panhysterectomy, Feb. 27. On March 6, 1939, temperature, respiration, and pulse rate normal; blood pressure 176/72. On March 7, sudden development of shock, with pain in upper left chest, present only on inspiration and later aggravated by inspiration, and a cold, clammy, cyanotic skin. At this time pulse rate was 132, blood pressure 88/60, blood sugar 280 mg. per cent; no cough or bloody sputum. One hour later, blood pressure rose to 125/85, and patient appeared normal except for residual dyspnea and inspiratory pain. *B* and *C*, March 7 and March 9. At this time temperature was 100° F., and, next day, 101.2° F. *D* and *E*, March 10 and March 15; roentgenogram of chest negative at this time; *F*, March 23. On March 24, 1939 pain reappeared in left upper chest, worse on breathing and sticking in character; chest normal on physical examination, and temperature 101.2° F. that night. *G*, April 12, 1939. Patient survived.

nary embolism more probable. However, it must be remembered that some patients show none of these signs, and the diagnosis must therefore be made without them.

The previous state of the heart apparently does not affect in any uniform manner the electrocardiographic changes produced by pulmonary embolism. Thus, instances falling into the group in which there were no notable abnormalities were seen in patients with and without coronary sclerosis. Patients with hypertensive cardiovascular disease who had an abnormal electrocardiogram before embolism occurred may show no further change afterward, and pulmonary embolism may not modify the electrocardiographic alterations produced by recent myocardial infarction.

POSSIBLE MECHANISMS INVOLVED IN THE PRODUCTION OF ELECTROCARDIOGRAPHIC CHANGES

The mechanism of the production of the electrocardiographic changes is obscure. Many authors have commented on the lack of correlation between the size of the embolus and the clinical manifestations (Scherf and Schonbrunner,[3] de Takats, et al.[13]). Emboli too small to obstruct the principal pulmonary vessels have proved to be rapidly fatal. Therefore, reflexes have been invoked to account for this discrepancy. Villaret, et al.,[14] in studying experimental embolism in dogs, found that, after bilateral vagotomy, seven times the usual lethal dose of seeds was necessary to cause death. De Takats, et al.,[13] using a standard $FeCl_3$ and $BaSO_4$ emulsion, found that about half of their dogs could be saved after a dose which was ordinarily fatal, either by vagotomy or by giving atropine and papaverine intravenously. Both groups of investigators observed that sympathectomy or adrenalin produced just the opposite effect. Scherf and Schonbrunner[3] postulated a pulmonovagal reflex constriction of the coronary vessels, and attributed the electrocardiographic changes to an impairment in the nutrition of the heart produced by this constriction. However, the work of Katz and Jochim[15] on the dog did not substantiate this view, for they found that the vagal nerve fibers actually produce coronary vasodilatation.

A more plausible explanation of the disproportion between the electrocardiographic changes and the clinical manifestations when the emboli are small, for which there is still no proof, is that there may be a reflex vasoconstriction of the remaining pulmonary vascular bed. In this way, the effect of massive pulmonary obstruction would be simulated. The tachypnea, however, is probably caused by a direct reflex action upon the respiratory center, as the work of de Takats, et al.,[13] indicates. Experimental massive pulmonary embolism has been shown by Mendlowitz[16] to cause the heart to dissipate its energy in overcoming the obstruction, leading to circulatory failure. In this way, a relative myocardial ischemia, produced purely dynamically, might give rise to the transitory electrocardiographic changes. This ischemia is due to a relative increase

in work and energy consumption of the heart compared to the coronary flow. The elevated pressure in the right heart, acting as an obstruction to coronary venous drainage, is the primary mechanism slowing coronary flow when the systemic arterial blood pressure does not fall (see Katz, Jochim, and Bohning[17]). The wide distribution of the ischemia might produce, in the limb leads, a contour resembling that seen in posterior wall infarction, but with a tendency toward S-T depressions, while the chest leads would assume the contour characteristic of anterior wall infarction. Also, death can be attributed to the fact that the myocardial ischemia causes the right ventricle to fail to meet the acute load of the pulmonary obstruction. It might also result from ventricular fibrillation, since prefibrillatory arrhythmias do develop.

SUMMARY

Fifty cases of pulmonary embolism (including twenty-seven autopsy cases) were studied in order to ascertain the kind of electrocardiographic changes produced and their relative frequency. It was found that no constant abnormality occurred, and that a large percentage of patients had either normal, nonspecific changes of no diagnostic significance, or no alteration in abnormalities which antedated the embolism. The distinctive electrocardiographic manifestations described by McGinn and White[1] were encountered, but they were rather infrequent (10 per cent of cases). More frequent were S-T deviations, particularly depression in Leads I and II, and T-wave inversion in Leads III and CF_2. This is in accord with the observations of Love, et al.[5] In the limb leads these changes roughly simulate those of posterior infarction (depression of $S\text{-}T_1$ and $S\text{-}T_2$, with elevation of $S\text{-}T_3$ and inversion of T_3, as well as the presence of Q_3 and S_1) and, in the chest leads, those of anterior infarction (slight elevation of S-T in CF_2, inversion of T in CF_2, with a diphasic QRS in CF_2). A discussion of the means by which the electrocardiographic changes in pulmonary embolism may be differentiated from those of myocardial infarction is presented. In a few cases serial curves after pulmonary embolism are shown. The lack of a characteristic evolutionary pattern demonstrated the greater utility of CF_2 over CF_4 and therefore also IVF is demonstrated.

The diagnosis of pulmonary embolism, it appears to us, must rest on an awareness of its possibility, and the suspicion that it may be present when atypical electrocardiographic features which superficially resemble coronary occlusion are noted. A careful correlation of the clinical and electrocardiographic manifestations is essential for the diagnosis.

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STUDIES IN HYPERTENSIVE HEART DISEASE

I. The Incidence of Coronary Atherosclerosis in Cases of Essential Hypertension

David Davis, M.D., and Max J. Klainer, M.D.
Boston, Mass.

IT HAS been shown that patients with essential hypertension show a comparatively high incidence of coronary atherosclerosis.[1, 2, 3] The magnitude of the change and its relation to age and sex, however, have not been firmly established. Our purpose is to present more data on this aspect of the problem.

METHOD

The degree of coronary atherosclerosis was estimated in patients with essential hypertension and in a control series of patients of corresponding age and sex who did not have hypertension.

Sources of Error.—An attempt was made to avoid the following errors, encountered in the literature:

(1) The assumption that, in the absence of valvular disease, the presence of cardiac hypertrophy at necropsy is evidence of past hypertension.[1, 2] It has been shown that cardiac hypertrophy which is not secondary to valvular disease may be due to causes other than hypertension.[4] Therefore, the diagnosis of essential hypertension was based entirely on clinical data.

(2) A diagnosis of hypertension based on blood pressure measurements made during the terminal illness. As such measurements are often unreliable, all patients used in the present study had repeated blood pressure readings prior to the terminal illness.

(3) The inclusion of patients with hypertension of renal origin. We have shown that patients with hypertension secondary to primary nephritis, who die in uremia, do not show an increased incidence of coronary disease.[5] Such cases were therefore excluded.

(4) The inclusion of diabetic patients. The incidence of coronary disease is relatively high in diabetic patients, even in the absence of hypertension. Therefore, these patients were excluded from the series.

(5) The failure to control age and sex factors. Coronary disease increases with age, and its clinical manifestations occur much less frequently in women than in men. In comparing patients with hypertension with the controls, it was therefore important that both groups show a comparable age and sex distribution.

Furthermore, in studying necropsy data, one must beware of certain errors that are found in autopsy protocols. It is recognized that notes on the coronary vessels which are made during routine necropsies may not always be reliable. When the cause of death is extracardiac, the coronary vessels may not be examined with sufficient care to ascertain the extent of the atherosclerotic lesions, if any are present. If sufficient care is taken, i.e., if the three main coronary arteries are opened throughout their entire length, accurate data on the condition of these vessels can be obtained by routine dissection alone, in most cases. This

From the Medical Research Laboratories of the Beth Israel Hospital, and the Department of Medicine, Harvard Medical School, Boston.
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is particularly true of marked changes, such as the presence or absence of significant narrowing or occlusion. We were able to form some idea of the accuracy of routine dissection by comparing data secured by that means with those obtained by the injection-dissection method of Schlesinger.[6] With this method the coronary vessels are first injected with liquid agar containing an opaque substance for radiographic purposes and a dye to facilitate dissection. The heart is then opened in a unique manner, so that the three major vessels can be roentgenographed as they lie in one plane, and, finally, the coronary arteries are dissected with the guidance of the roentgenogram.

Selection of Cases.—Data on the condition of the coronary vessels in 407 cases were obtained from routine necropsy protocols. In 100 additional cases they were obtained by the injection-dissection technique. These cases were consecutive and unselected except for the exclusion of cases of rheumatic and syphilitic heart disease, diabetes, myxedema, and hyperthyroidism, i.e., diseases which themselves affect either the heart or the coronary vessels. A further small group of cases was excluded because the presence or absence of hypertension could not be conclusively established. The five hundred seven cases which remained were then arbitrarily divided into three groups. The first group of 137 patients were classified, on the basis of the clinical and pathologic findings, as instances of essential hypertension; the hearts of twenty-two of these were studied by injection and dissection. A patient was considered to have hypertension when the systolic blood pressure was consistently above 150, and the diastolic consistently above 90, millimeters of mercury, on one or more admissions prior to the terminal illness. The systolic pressures varied from 150 to 180, and the diastolic from 90 to 100, in thirteen patients; from 180 to 220, systolic, and 100 to 120, diastolic, in sixty-eight patients; and in the remaining fifty-six cases the pressure was consistently above these levels. No patient in this group had extensive, primary, renal disease. A second group, not considered in this study, comprised forty-six patients, all of whom had hypertension, died of uremia, and had severe, primary, renal disease, such as glomerulonephritis, pyelonephritis, and polycystic kidneys. The remaining 324 cases served as controls. These patients, in every instance, had a record of normal blood pressure before the terminal illness; the hearts of sixty-eight of them were studied by the Schlesinger technique.

Criteria for Coronary Disease.—The degree of coronary sclerosis was ascertained from the description in the protocols. When it was stated that the intima of the coronary vessels was smooth and essentially free from atheromatous plaques, the degree of coronary sclerosis was classified as grade I; grade II included cases in which there were scattered atheromatous plaques; grade III, cases in which the greater part of the intimal surface was covered with atheromatous plaques, and there was little or no narrowing of the lumen; grade IV, cases in which there was moderate to marked narrowing, or an occlusion, of one of the major coronary branches; and grade V, cases in which there were an occlusion of one, and extensive disease or occlusion of at least one other, of the three major arteries. For purposes of analysis, grades I and II were classified as slight, grade III as moderate, and grades IV and V as marked, coronary disease.

ANALYSIS OF DATA

One hundred thirty-seven patients with essential hypertension (90 males, 47 females) and 324 controls (230 males, 94 females) were available for analysis.

Table I compares the occurrence of coronary disease in essential hypertension with that in patients of the same age without hypertension. At all ages, a significantly higher incidence of coronary sclerosis was

noted in the patients with hypertension (Table I, Chart I). On the other hand, the incidence of slight coronary disease was much higher in patients without hypertension (Table I, Chart II). The percentage of cases of hypertension in which there was marked coronary disease was as high before, as it was after, the age of 50 (Table II). Between the ages of 30 and 49 years, the incidence of severe disease in controls and in patients with hypertension was 15 per cent and 44 per cent, respectively, and at the age of 70, or more, 32 per cent and 44 per cent,

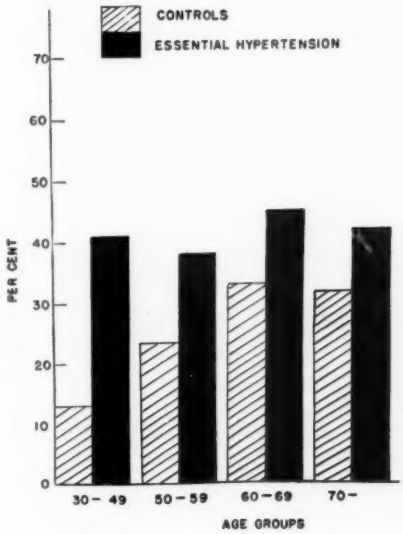

Chart I.—Incidence of severe coronary disease.

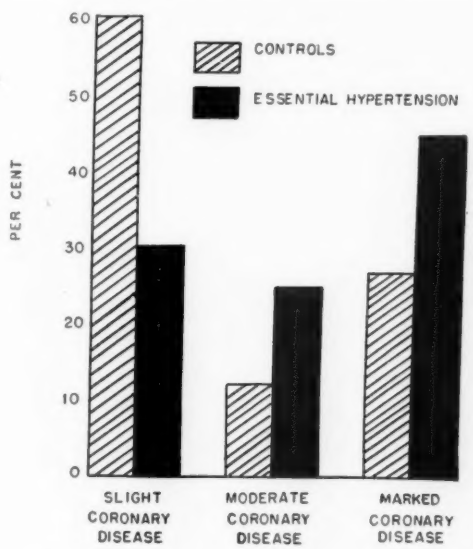

Chart II.—Incidence of coronary disease.

respectively. The average for the six decades for patients with hypertension was 45 per cent; for the controls, 27 per cent, an increase over controls of 76 per cent.

It was of interest to ascertain whether or not the same tendency would be manifest in the small group of cases in which the hearts were studied by the injection-dissection technique. As one would expect with the more accurate method, a somewhat higher incidence of severe coronary disease was found both in the patients with hypertension and in the controls. In order to ascertain the relative accuracy of protocol data, we compared (Table III) the degree of coronary sclerosis in the injected

TABLE I

THE INCIDENCE OF CORONARY ATHEROSCLEROSIS IN PATIENTS WITH AND WITHOUT HYPERTENSION ACCORDING TO DECADES

DECADE	CLASSIFICATION	TOTAL NO. OF CASES	SLIGHT CORONARY DISEASE		MODERATE CORONARY DISEASE		MARKED CORONARY DISEASE	
			CASES	PER CENT	CASES	PER CENT	CASES	PER CENT
30-39	Patients with hypertension	3	1	33.3	1	33.3	1	33.3
	Controls	21	19	90.5	0		2	9.5
40-49	Patients with hypertension	13	6	46.2	1	7.6	6	46.2
	Controls	47	37	78.7	2	4.3	8	17.0
50-59	Patients with hypertension	29	8	27.6	10	34.5	11	37.9
	Controls	85	56	65.9	9	10.6	20	23.5
60-69	Patients with hypertension	49	14	28.5	13	26.5	22	45.0
	Controls	96	49	51.0	16	16.7	31	32.3
70-79	Patients with hypertension	37	11	29.6	12	32.4	14	38.0
	Controls	43	26	60.4	6	14.0	11	25.6
80-	Patients with hypertension	6	1	16.6	1	16.6	4	66.7
	Controls	11	2	18.2	3	27.3	6	54.5
Average of decades	Patients with hypertension	137	41	30.2	38	25.2	58	44.7
	Controls	303	189	60.8	36	12.1	78	27.1

TABLE II

THE INCIDENCE OF MARKED CORONARY DISEASE IN PATIENTS WITH AND WITHOUT HYPERTENSION ACCORDING TO DECADES

DECADE	PATIENTS WITHOUT HYPERTENSION		PER CENT	20-YEAR PERIOD	PATIENTS WITH HYPERTENSION		PER CENT	20-YEAR PERIOD	DIFFERENCE IN INCIDENCE (PER CENT)
	TOTAL NO. OF CASES	SEVERE COR. DIS.			TOTAL NO. OF CASES	SEVERE COR. DIS.			
30-39	21	2	9.5	14.9	3	1	33.3	43.8	198
40-49	47	8	17.0		13	6	47.2		
50-59	85	20	23.5	28.2	29	11	37.9	42.3	50
60-69	96	31	32.3		49	22	45.0		
70-79	43	11	25.6	31.5	37	14	38.0	44.4	41
80-	11	6	54.5		6	4	66.7		

and noninjected hearts of patients without hypertension. The ages in the group ranged from 50 to 69, for only in this period was there a sufficient number of injected hearts for comparison. In the noninjected hearts the incidence of slight, moderate, and marked coronary disease was 58 per cent, 16 per cent, and 26 per cent, respectively. In the injected hearts the incidence was 56 per cent, 8 per cent, and 36 per cent, respectively. Apparently, the injection technique reveals a higher incidence of marked narrowing and occlusion. This error, however, occurred both in cases of hypertension and in the controls. Actually, the incidence of severe coronary disease in the twenty-two injected hearts from patients who had had hypertension was 63 per cent greater than in the sixty-eight injected hearts from patients who had not had hypertension, which is approximately the same as the proportion in the entire group.

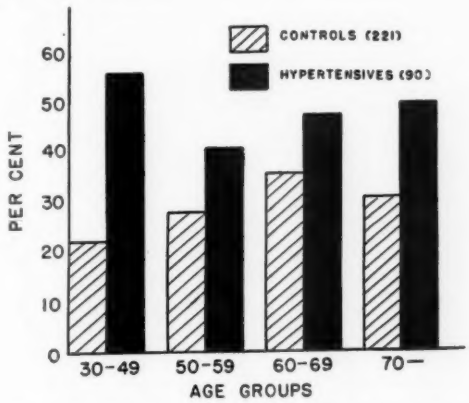

Chart III.—Marked coronary disease in males.

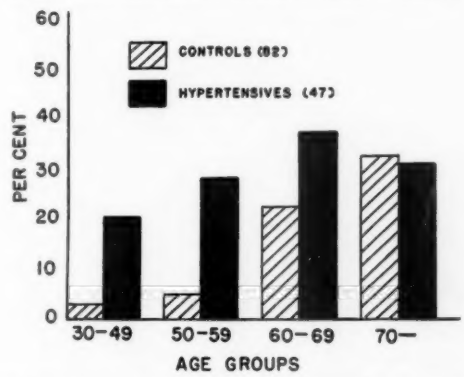

Chart IV.—Marked coronary disease in females.

The relation of coronary disease to sex.—In persons who had not had hypertension, the incidence of marked coronary disease at necropsy was much greater in men than in women, particularly below the age of 60; its occurrence in women under 60 was very infrequent (Table IV).

Above this age there is a rapid rise, so that, after 70, marked coronary disease is found as frequently in women as in men.

The incidence of coronary disease in men and women with hypertension is seen in Table V. Although the incidence of coronary disease is increased in women with hypertension, it is still considerably below that in men with hypertension (Charts III and IV). The incidence of coronary disease in women with hypertension is about the same as that in men without hypertension.

DISCUSSION

In 1928, Bell and Clawson[1] and, more recently, Clawson[2] pointed out that the incidence of coronary disease is high in patients with hypertension, and their widely quoted investigations have been largely responsible for focusing attention on this fact. Because of certain criteria employed in the selection of their cases, however, the actual incidence of coronary disease cannot be ascertained from their data. The diagnosis of hypertension, for example, was based on the presence of cardiac hypertrophy at necropsy in 200 cases, and the only criterion for the diagnosis

TABLE III

THE INCIDENCE OF CORONARY ATHEROSCLEROSIS IN INJECTED AND NONINJECTED HEARTS FROM PATIENTS WHO HAD NOT HAD HYPERTENSION

AGE (YEARS)	CLASSIFICATION	NO. OF CASES	CORONARY DISEASE					
			SLIGHT		MODERATE		SEVERE	
50-69	Injected hearts	39	22	56.4%	3	7.7%	14	35.9%
	Noninjected hearts	142	83	58.4%	22	15.5%	37	26.1%
	Combined	181	105	58.0%	25	13.8%	51	28.2%

TABLE IV

THE INCIDENCE OF MARKED CORONARY DISEASE IN MEN AND WOMEN WHO HAD NOT HAD HYPERTENSION

AGE (YEARS)	SEX	TOTAL NO. OF CASES	MARKED CORONARY DISEASE	
			NO. OF CASES	PER CENT
30-49	Male	41	9	21.9
	Female	27	1	3.7
50-59	Male	65	19	29.2
	Female	20	1	5.0
60-69	Male	73	26	35.6
	Female	23	5	21.7
70-	Male	42	13	30.9
	Female	12	4	33.3
Average	Male	221	67	30.3
	Female	82	11	13.4

of hypertension in the remaining 220 cases of their series was a systolic pressure of 150, or more, millimeters of mercury. It has been shown recently that, in the absence of valvular disease, hypertrophy may be caused by congestive heart failure,[4] and, inasmuch as congestive heart

TABLE V

THE INCIDENCE OF MARKED CORONARY DISEASE IN MEN AND WOMEN WHO HAD HAD HYPERTENSION

AGE (YEARS)	SEX	TOTAL NO. OF CASES	MARKED CORONARY DISEASE	
			NO. OF CASES	PER CENT
30-49	Males	11	6	55.4
	Females	5	1	20.0
50-59	Males	22	9	40.9
	Females	7	2	28.6
60-69	Males	33	16	48.5
	Females	16	6	37.5
70-	Males	24	12	50.0
	Females	19	6	31.6
Average	Males	90	43	47.8
	Females	47	15	31.9

failure was present in 187 of their cases, the importance of this source of error cannot be overlooked. This is especially true because patients with heart failure which is not secondary to hypertension or valvular disease show a very high incidence of coronary disease.[7] Furthermore, 5 per cent of the patients in their series were diabetics. In 1934, Murphy and his co-workers[3] studied the same problem, and likewise demonstrated a high incidence of coronary disease in this condition.

The present analysis shows the incidence of coronary disease at necropsy in patients of various ages. A strikingly high incidence of marked coronary disease was found in patients with hypertension under the age of 50 (Table II). On the average, the incidence exceeded that in patients without hypertension, at all ages, by 76 per cent. As will be shown in a subsequent publication, there was no relationship between the degree of coronary disease and the degree of hypertension or cardiac hypertrophy in these cases.[5]

In conformity with other observations on the clinical manifestations of coronary disease in men and women, there was a low incidence of coronary disease in women who did not have hypertension. The rarity of angina pectoris in women below the age of 50 who do not have hypertension or diabetes has recently been stressed by Levy and Boas.[8] Our data suggest that it is uncommon even in the sixth decade. Above the age of 60, the incidence of coronary disease increases rapidly, and after 70 its occurrence is approximately the same in men and women who do not have hypertension.

It is known that hypertension is much more common in women than in men,[9] and because of the high incidence of coronary sclerosis in cases of hypertension, one would at first expect a high incidence of coronary disease in women with hypertension. Although they do have more coronary disease than women without hypertension, at all ages, the difference between men and women with hypertension is still significant. Actually, women with hypertension show the same incidence of coronary disease as men without hypertension (Charts III, IV).

CONCLUSIONS

1. Patients with essential hypertension have more coronary atherosclerosis than patients without hypertension; the difference in incidence amounts to approximately 76 per cent.

2. The difference is particularly striking before the age of 50.

3. Men without hypertension have much more coronary disease than women without hypertension, especially before the age of 60.

4. Essential hypertension increases the incidence of coronary atherosclerosis proportionately in both sexes.

5. In spite of the higher incidence of hypertension in women, the degree of coronary atherosclerosis in women with hypertension remains significantly lower than that in men with hypertension. The actual incidence of severe coronary sclerosis in women with hypertension approximates that in men without hypertension.

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STUDIES IN HYPERTENSIVE HEART DISEASE

II. The Role of Hypertension, per se, in the Development of Coronary Sclerosis

David Davis, M.D., and Max J. Klainer, M.D.
Boston, Mass.

THE relatively high incidence of coronary atherosclerosis in cases of essential hypertension has been attributed to the effect of the elevated pressure on the blood vessel walls. If this be true, patients with severe hypertension would be expected to have more marked coronary atherosclerosis than those with mild hypertension of the same duration, and patients with hypertension of renal origin should have more coronary disease than patients with no hypertension. In this paper data will be presented to show that the elevated pressure, per se, is not the most important factor in the production of coronary disease.

METHOD

The way in which cases were selected and the criteria of coronary disease were discussed in the first paper of this series.[1] There were 137 patients with essential hypertension, forty-six with hypertension of renal origin, and 324 in the control series of patients without hypertension.

The relation of the severity of hypertension to the degree of coronary disease.—In estimating the severity of hypertension in a given case, two factors have to be considered: (1) the average height of the blood pressure, and (2) the duration of the hypertension. It was not possible to ascertain the duration of the hypertension in most of our patients, although there was a history or record of hypertension of ten or more years' duration in seventeen cases. It may be assumed, however, that, for a given age, the duration of the hypertension in patients with high blood pressure is at least as long as it is in patients with lower pressures.[2] All forms of hypertension, however, regularly lead to cardiac hypertrophy and, in the absence of congestive failure, this is related both to the duration and the degree of the hypertension. It has been shown that severe coronary sclerosis, per se, may produce only a slight degree of cardiac hypertrophy.[3] Therefore, the weight of the heart post mortem is perhaps a better indication of the severity of the hypertension. Thus we used two criteria for estimating the effect of hypertension on the circulation: (1) the general level of the blood pressure before the final illness, and (2) the weight of the heart at necropsy.

From the Medical Research Laboratories of the Beth Israel Hospital, and the Department of Medicine, Harvard Medical School, Boston.
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Our data show that the incidence of marked coronary disease is the same in cases of mild and severe hypertension (Table I, Chart I). There is a similar lack of correlation between heart weights and the degree of coronary disease (Table II). Of the cases in which the heart weights were below 450 grams, there was marked coronary disease in 41.3 per cent, and in the cases in which the heart weights were above 550 grams, the incidence was 41.8 per cent. Cases of heart failure, or calcification of the aortic ring, with stenosis, were, of course, excluded from this tabulation, as either may produce appreciable cardiac hypertrophy without hypertension.[3]

TABLE I

THE RELATION OF BLOOD PRESSURE LEVELS TO CORONARY DISEASE

B.P. LEVELS	NO. TOTAL	SLIGHT COR. DIS.		MODERATE COR. DIS.		MARKED COR. DIS.	
		CASES	%	CASES	%	CASES	%
150/90-180/100	13	4	30.7	2	15.4	7	53.9
180/100-220/120	68	20	29.4	20	29.4	28	41.2
220/120-	56	17	30.4	15	26.7	24	42.9

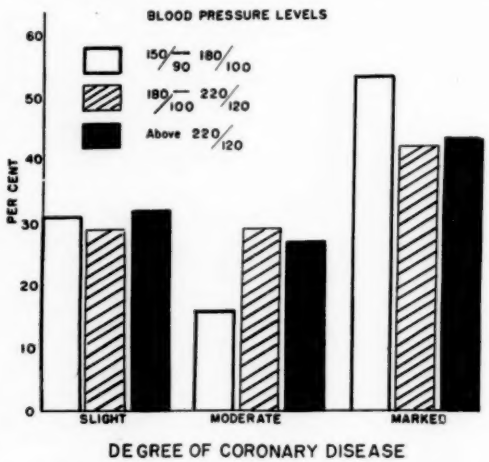

Chart I.—Relation of the severity of hypertension to coronary atherosclerosis.

The incidence of coronary disease in patients with hypertension of renal origin and in a control series of patients without hypertension. The incidence and degree of coronary disease in the forty-six patients with hypertension of renal origin and in 270 controls of corresponding age are compared in Table III. All of these forty-six patients died in uremia, and, at necropsy, showed severe primary renal disease (Table V). Most of them had severe hypertension. In 61 per cent the systolic pressures were above 220 and the diastolic pressures above 120; in 33 per cent the pressures were between 180 to 220, systolic, and 100 to 120, diastolic. Fortunately, the hearts of ten of these forty-six patients were

TABLE II

HEART WEIGHT AND CORONARY DISEASE IN CASES OF ESSENTIAL HYPERTENSION

HT. WT. IN GM.	TOTAL NO.	SLIGHT COR. DIS.		MODERATE COR. DIS.		MARKED COR. DIS.	
		CASES	%	CASES	%	CASES	%
To 450	46	18	39.1	9	19.6	19	41.3
451-550	23	8	34.8	7	30.4	8	34.8
551-	27	8	29.6	8	29.6	11	41.8

TABLE III

INCIDENCE OF CORONARY SCLEROSIS IN CASES OF RENAL HYPERTENSION AND IN PATIENTS OF THE SAME AGE WHO DID NOT HAVE HYPERTENSION

AGE GROUP	CLASSIFICATION	TOTAL NO. OF CASES	NONE, TO SLIGHT, CORONARY DISEASE		MODERATE CORONARY DISEASE		MARKED CORONARY DISEASE	
			CASES	%	CASES	%	CASES	%
	Nephritics	8	7	87.5	1	12.5		
10-29	Controls	21	21	100.0	0			
	Nephritics	23	17	73.9	6	26.1	0	
30-49	Controls	68	56	82.3	2	3.0	10	14.7
	Nephritics	15	10	66.7	4	26.6	1	6.7
50-69	Controls	181	105	58.0	25	13.8	51	28.2

TABLE IV

HEART WEIGHT AND CORONARY DISEASE IN CASES OF RENAL HYPERTENSION

HT. WT. IN GM.	TOTAL NO. OF CASES	SLIGHT CORONARY DISEASE	MODERATE CORONARY DISEASE	MARKED CORONARY DISEASE
To 350	7	7	-	-
351-450	14	8	5	1
451-550	9	7	2	-
551-	11	7	4	-

TABLE V

CAUSES OF DEATH IN CASES OF RENAL HYPERTENSION

TYPE OF RENAL DISEASE	CASES	PER CENT
Chronic Glomerulonephritis	35	76.1
Subacute Glomerulonephritis	3	6.5
Congenitally Polycystic Kidneys	4	8.7
Hydronephrosis, Bilateral	2	4.3
Pyelonephritis, Bilateral	1	2.2
Atrophic Kidney, Unilateral	1	2.2

studied by the injection dissection method.[4] In not a single case in the entire group had occlusion of a major coronary vessel occurred, and in only one case was the degree of sclerosis graded as "marked," because of pronounced narrowing of the left anterior descending artery. In the control group, marked coronary disease was present in 22.6 per cent of the 270 hearts, sixty of which were studied by the Schlesinger technique.[4] In thirty-six of the sixty-one control cases, in which the sclerosis was classified as "marked," there were occlusions of one or more of the major coronary vessels; in twenty-one cases there was occlusion of one, in twelve of two, and in three of all three large coronary

arteries. In one of the control cases, in the fourth decade of life, there was occlusion of a major coronary vessel. In the fifth decade there were six control cases, or 12.8 per cent, in which occlusions of one or more major coronary arteries had occurred. It is of interest that none of the eleven patients with nephritis who were in the fourth decade, and none of the twelve in the fifth, showed any appreciable narrowing or occlusion of a coronary vessel (Table III).

This higher incidence of coronary atherosclerosis in the control patients is all the more remarkable because of the severity of the hypertension in the patients with nephritis, as evidenced both by the recorded blood pressure levels and the degree of cardiac hypertrophy at necropsy (Table IV).

DISCUSSION

When it was established that patients with essential hypertension show a high incidence of coronary disease,[1, 5, 6] the possibility that the increased pressure itself was a factor in its production was seriously entertained. The atherosclerotic changes with increasing age in individuals without hypertension were entirely consistent with this hypothesis, for these changes conceivably represented the accumulated effects of lower pressures over a period of many years. Our data, however, present evidence that hypertension, per se, is not the cause of the increased incidence of coronary atherosclerosis. Patients with severe hypertension, as evidenced both by the general blood pressure level during life and by the extent of cardiac hypertrophy at necropsy, did not have any more coronary disease than did patients with mild degrees of hypertension; patients with hypertension caused by primary renal disease actually showed less coronary disease than a corresponding group of patients who did not have hypertension.

The frequent association of coronary atherosclerosis with hypertension suggests that the two are independent results of a common etiologic factor. A plausible explanation for their association is the following: Atherosclerosis occurs, for reasons as yet unknown, in varying degrees in different individuals, and the distribution of the atherosclerotic process in a given individual is irregular. Such patients develop atherosclerosis of the coronary arteries, although the degree of involvement may not be sufficient to cause symptoms. If atherosclerosis develops in certain other parts of the body, permanent hypertension may result; interference with the blood supply to the kidneys[7] or to the brain[8] is known to produce hypertension. Interference with the blood supply to other structures, not yet studied, may do likewise. This hypothesis explains the occurrence of marked coronary disease without hypertension and the high incidence of coronary sclerosis in patients with hypertension. The same concept is in harmony with the recognized fact that hypertension and coronary sclerosis occur frequently in patients with diabetes.[9]

CONCLUSIONS

1. Evidence is offered to show that, although the incidence of coronary atherosclerosis in patients with essential hypertension is relatively high, hypertension, per se, is not the cause of this high incidence.

2. The relationship of hypertension to arteriosclerosis is discussed.

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STUDIES IN HYPERTENSIVE HEART DISEASE

III. Factors in the Production of Angina Pectoris

David Davis, M.D., and Max J. Klainer, M.D.
Boston, Mass.

AN IMPRESSIVE body of evidence points to myocardial anoxemia and ischemia as the probable causes of angina pectoris. Coronary insufficiency is now regarded as the major cause of such ischemia. The importance of aortic insufficiency, thyrotoxicosis, and anemia, as predisposing factors, has been stressed. From an analysis of the anatomic observations in a group of cases of angina pectoris associated with hypertension and a group without hypertension, it appears that other factors, not yet emphasized in the literature, play a role in the production of the anginal syndrome in cases of essential hypertension. The significance of these factors is discussed in the present communication.

The anatomic basis of angina pectoris, as disclosed by the very exact injection-dissection technique of Schlesinger,[1] has been described elsewhere. In the present study, routine autopsy protocols were used; admittedly, this method yields data which are less reliable than those made available by the above-mentioned technique. They have the advantage, however, of making possible a study of a much larger series of cases.

METHOD

The data used in the present analysis were based on a study of 137 patients with hypertension and 324 individuals without hypertension. Patients were considered to have hypertension when their systolic blood pressures were consistently above 150, and their diastolic consistently above 90, millimeters of mercury, on one or more occasions prior to the terminal illness. Coronary sclerosis was graded as slight (grade 1) when the intimal surface of the three major vessels was essentially smooth or marred only by a few scattered atheromatous plaques; moderate coronary disease (grade 2) was said to be present when the intimal surfaces were completely involved by the sclerotic process without appreciable narrowing of the lumen; and narrowing or occlusion of one or more of the three major arteries was classified as a marked degree of sclerosis (grade 3). Patients with diabetes, thyrotoxicosis, and myxedema, and rheumatic, syphilitic, or congenital heart disease were excluded from this study.

Angina pectoris was present in forty patients with nonvalvular hypertensive heart disease, and in twenty-one with nonvalvular heart disease unassociated with hypertension. The diagnosis was based on a record of definite attacks of substernal or precordial pain, which were precipitated by exertion and relieved by rest or nitroglycerin. Attacks of pain in the left side of the chest not answering to this description were excluded.

From the Medical Research Laboratories of the Beth Israel Hospital, and the Department of Medicine, Harvard Medical School, Boston.
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ANALYSIS OF DATA

Comparison of patients with and without hypertension.

Sex.—The large proportion of men in both groups is striking, and is in conformity with the known incidence of coronary disease in men and women.[2] Of the sixty-one patients with angina pectoris, both with and without hypertension, only 60 per cent of the men with angina pectoris had hypertension, whereas 90 per cent of the women with angina had elevated blood pressures. There were fifty-two men and nine women.

Congestive failure.—The incidence of congestive failure during the course of angina pectoris was 72 per cent in both groups. Four patients with hypertension and two without hypertension had their first attacks of angina pectoris during periods of cardiac decompensation. The duration of life after the development of congestive failure appeared to be somewhat longer in the cases in which there was no hypertension (Tables II, III).

Coronary disease.—The frequency of marked coronary disease, as exemplified by the occurrence of coronary occlusions, was significantly higher in the patients without hypertension. Only twenty-two, or 55 per cent, of the patients with hypertension had occlusions of one or more major coronary branches, whereas in nineteen, or 90 per cent, of

TABLE I

PATIENTS WITH ANGINA PECTORIS

DATA	WITH HYPERTENSION		WITHOUT HYPERTENSION	
TOTAL CASES	40	100%	21	100%
Age Distribution				
30-49 years	5	12.5%	2	9.6%
50-59 years	11	27.5%	6	28.5%
60-69 years	16	40.0%	12	57.1%
70- years	8	20.0%	1	4.8%
Sex				
Males	32	80.0%	20	95.2%
Females	8	20.0%	1	4.8%
Angina Pectoris prior to C. F.	36	90.0%	19	90.4%
Angina Pectoris after C. F.	4	10.0%	2	9.6%
Congestive Failure (C. F.) during course of Angina Pectoris	29	72.5%	15	71.8%
Cases of Coronary Occlusion	22	55.0%	19	90.4%
Cases of Cardiac Infarction	15	37.5%	17	81.0%
Old Infarcts	7	17.5%	10	47.6%
Recent Infarcts	8	20.0%	7	33.3%

the cases of angina pectoris without hypertension such occlusions occurred. The coronary branches involved in each group were approximately the same.

Myocardial infarction.—The incidence of infarcts was likewise considerably lower in the cases of hypertension, and corresponded closely with the frequency of marked coronary disease in these two groups.

Only fifteen, or 38 per cent, of the patients with hypertension had either old or recent infarcts, whereas seventeen, or 81 per cent, of the patients without hypertension were found to have infarcts.

DISCUSSION

Since Jenner first demonstrated that coronary disease is an important factor in the production of Heberden's angina pectoris,[3] there has been much discussion as to its significance. It was recognized, however, that there was not always a close parallelism between the degree of coronary sclerosis and angina pectoris. The possible role of aortic disease was suggested by the occurrence of the anginal syndrome in patients with aortitis or aortic valve lesions. Later it was observed that attacks of angina pectoris occurred, without severe coronary disease, in patients with chronic anemia, congestive failure, and an increased metabolic rate, all of which predispose to myocardial ischemia and anoxemia, which, in turn, are regarded as the underlying cause of angina pectoris.[4, 5, 6]

The data here presented demonstrate the importance of other factors which predispose to acute myocardial anoxia and angina pectoris.

Angina pectoris in nonhypertensive heart disease.—It will be noted that extensive coronary disease, with occlusion of one or more major vessels, was present in nineteen of the twenty-one patients with angina pectoris in this group; six patients had occlusions in two, and four patients had occlusions in all three, major branches (Table II). In Case 20 there was only a slight amount of coronary sclerosis, but this patient had myelogenous leucemia and a marked secondary anemia; the latter undoubtedly favored the occurrence of myocardial anoxia. In Case 21 there was a history of right-sided congestive failure of two years' duration, caused by cor pulmonale. The anoxemia of congestive failure and pulmonary disease favored the occurrence of angina pectoris in this patient, in the absence of marked coronary sclerosis. Thus, in patients without hypertension, angina pectoris unassociated with anemia or congestive failure was invariably caused by extensive coronary disease.

Angina pectoris in hypertensive heart disease.—In contrast to these observations is the fact that the degree of coronary sclerosis was graded slight in five, and moderate in six, of a total of forty cases of angina pectoris associated with hypertensive heart disease. In twenty-nine cases the sclerosis was classified as marked, but in only twenty-two were there occlusions of major coronary vessels. In the majority of these twenty-nine patients the degree of coronary disease was less than that in the patients without hypertension. Severe atherosclerosis of two large coronary vessels was present in eighteen out of nineteen patients without hypertension, and in only nineteen of the twenty-nine patients with hypertension and severe coronary disease. In three of the eleven patients without marked coronary sclerosis, angina pectoris appeared

TABLE II

PATIENTS WITHOUT HYPERTENSION MANIFESTING ANGINA PECTORIS

NO.	AGE AND SEX	HEART WEIGHT	DEGREE COR. DIS.	VESSELS OCCLUDED			INFARCTS		DURATION OF ANGINA	CLINICALLY, CORONARY THROMBOSIS	C.F.	CAUSE OF DEATH
				L.A.D.	L.C.	R.C.	OLD	RECENT				
1	59 M	500	3	+	+	+	+	0	1 yr.	+	1 yr.	C.F.
2	64 M	400	3	+	0	+	0	+	8 yr.	+	0	C.T.
3	55 M	490	3	+	N	+	0	+	3 mo.	+	3 wk.	C.T.
4	46 M	410	3	+	+	0	0	+	2 mo.	+	0	C.T.
5	67 M	540	3	+	N	N	*	*	10 yr.	+	2 yr.	C.F.
6	68 M	580	3	+	+	+	*	*	5 yr.	+	3 yr.	C.F.
7	65 M	360	3	+	+	0	*	*	6 yr.	+	Terminal	C.T.
8	53 M	440	3	+	0	0	0	+	3 yr.	0	0	N.C.
9	65 M	450	3	+	N	0	+	0	8 mo.	+	6 mo.	C.T.
10	60 M	420	3	+	N	N	0	+	1 mo.	+	3 wk.	C.T.
11	63 M	620	3	N	+	0	+	0	2 yr.	0	2 yr.	C.F.
12	67 M	320	3	+	+	+	+	0	9 yr.	0	0	N.C.
13	49 M	420	3	+	N	N	+	0	4 yr.	+	0	N.C.
14	53 M	350	3	+	+	+	+	0	10 yr.	+	Terminal	C.T.
15	50 M	430	3	0	+	0	0	+	6 yr.	+	Terminal	C.T.
16	62 M	500	3	+	+	0	+	0	10 yr.	+	1 yr.	C.F.
17	80 M	530	3	+	N	0	0	0	14 mo.	0	3 yr.	C.F.
18	63 F	280	3	+	0	+	0	+	3 yr.	+	Terminal	C.T.
19	64 M	520	3	0	+	+	+	0	2 yr.	0	1 yr.	N.C.
20	54 M	490	1	0	0	0	0	0	7 wk.	0	0	N.C.
21	60 M	420	1	0	0	0	0	0	6 wk.	0	2 yr.	C.F.

* = diffuse fibrosis present
1 = slight, 2 = moderate, 3 = marked
N = significant narrowing
C.F. = congestive failure
C.T. = coronary thrombosis
N.C. = noncardiac

TABLE III

CASES OF ESSENTIAL HYPERTENSION IN WHICH THERE WAS ANGINA PECTORIS

NO.	AGE AND SEX	HEART WEIGHT	DEGREE COR. DIS.	VESSELS OCCLUDED			INFARCTS		DURATION OF ANGINA	CLINICALLY, CORONARY THROMBOSIS	C.F.	CAUSE OF DEATH
				L.A.D.	L.C.	R.C.	OLD	RECENT				
1	64 M	840	1	0	0	0	0	0	Few mo.	0	3-4 yr.	C.F.
2	64 M	620	1	0	0	0	0	0	3 yr.	0	0	N.C.
3	63 M	600	1	0	0	0	0	0	1 yr.	0	1 yr.	C.F.
4	63 F	360	1	0	0	0	0	0	3 yr.	0	3 mo.	N.C.
5	56 M	425	1	0	0	0	0	0	Few mo.	0	0	N.C.
6	75 M	400	2	0	0	0	*	*	19 yr.	+	1 yr.	C.F.
7	68 M	620	2	0	0	0	*	*	2 yr.	0	1 yr.	C.F.
8	77 M	800	2	0	0	0	0	0	1 yr.	?	4 mo.	C.F.
9	54 M	675	2	0	0	0	*	*	2 yr.	0	0	N.C.
10	58 M	450	2	0	0	0	0	0	2 mo.	?	Terminal	C.F.
11	63 M	640	2	0	0	0	0	0	10 mo.	0	1 yr.	C.F.
12	65 M	Large	3	N	0	0	0	0	8 yr.	0	0	N.C.
13	60 F	390	3	N	0	N	*	*	6 yr.	+	1 yr.	N.C.
14	73 F	460	3	0	0	N	0	0	1 yr.	+	Terminal	N.C.

* = diffuse fibrosis present
1 = slight, 2 = moderate, 3 = marked
N = significant narrowing
C.F. = congestive failure
C.T. = coronary thrombosis
N.C. = noncardiac

15	45 M	670	3	N	0	N	0	0	6 mo.	+	Few wk.	C.F.
16	59 M	1000	3	N	N	N	0	0	2 yr.	0	6-7 yr.	C.F.
17	59 F	480	3	N	N	N	+	0	1 yr.	+	0	C.T.
18	61 M	450	3	N	N	N	+	0	2 wk.	+	Terminal	C.T.
19	43 M	650	3	N	+	0	0	0	3 mo.	0	Few wk.	C.F.
20	67 M	440	3	+	0	0	0	0	2 wk.	+	2 yr.	C.F.
21	60 F	440	3	0	0	+	0	+	3 yr.	+	Terminal	C.T.
22	54 F	480	3	+	0	+	+	0	2 yr.	0	1 yr.	C.F.
23	60 F	510	3	+	+	+	0	0	5 yr.	+	Few wk.	C.T.
24	68 M	380	3	0	+	+	+	0	3½ yr.	0	0	N.C.
25	75 M	490	3	N	0	+	+	0	4 mo.	+	2 mo.	C.F.
26	64 M	510	3	+	0	+	0	+	8 yr.	+	Terminal	C.T.
27	68 M	620	3	+	0	0	+	0	9 yr.	+	Few wk.	C.T.
28	59 M	610	3	+	+	+	0	0	9 yr.	+	Terminal	C.F.
29	82 M	580	3	N	+	0	0	+	1 yr.	+	1 yr.	C.F.
30	49 M	600	3	+	N	0	+	0	5 yr.	0	0	N.C.
31	39 M	400	3	0	+	N	0	+	3 mo.	+	Terminal	C.T.
32	51 M	640	3	+	0	0	0	+	2½ yr.	+	Few wk.	C.T.
33	75 F	430	3	+	N	N	0	+	2 wk.	+	Terminal	C.T.
34	43 M	610	3	N	+	0	0	0	4 mo.	+	0	C.T.
35	74 M	600	3	+	+	0	0	+	31 yr.	+	4 yr.	C.F.
36	58 M	500	3	+	N	0	0	0	6 yr.	+	Terminal	C.T.
37	70 M	600	3	+	0	0	0	0	4 mo.	0	1 mo.	C.F.
38	52 M	880	3	+	0	0	0	+	8 yr.	+	Terminal	C.T.
39	67 M	520	3	+	0	0	0	0	3 mo.	0	2 mo.	N.C.
40	58 M	560	3	0	0	+	0	0	3 yr.	?	0	C.T.?

after the onset of congestive failure. This, however, was not the case in the remaining eight. Five of these eight patients had blood pressure levels which were consistently above 180, systolic, and 100, diastolic. The remaining three patients had pressures above 220, systolic, and 120, diastolic.

It is clear that hypertensive heart disease predisposes to attacks of angina pectoris in patients with lesser degrees of coronary sclerosis.

Two factors which were present in these patients and may have favored the occurrence of angina were (1) cardiac hypertrophy and (2) increased cardiac work. It has been suggested by Wearn[8] that cardiac hypertrophy interferes with the nutrition of the heart muscle, for the number of capillaries remains unchanged in spite of the increase in muscle mass. Harrison[9] has pointed out that oxygen diffusion into muscle fibers is probably impaired when the muscle fibers increase in thickness. A considerable degree of cardiac hypertrophy was present in 80 per cent of our cases of hypertension (Table III). Congestive failure itself is a factor in the production of hypertrophy,[10] so that in many of these cases it was impossible to ascertain how much of the hypertrophy was caused by the hypertension alone. Nine patients, however, died without having congestive failure, and in ten others it was a terminal phenomenon. Of eight patients with angina pectoris unassociated with severe coronary disease (Cases 2 and 4 to 10), the hearts in five were markedly hypertrophied, weighing from 600 to 840 grams at necropsy. In these cases hypertrophy was probably an important factor in the production of the anginal syndrome. In Cases 4, 5, and 6, on the other hand, there was but slight cardiac hypertrophy; there was no obvious anatomic explanation for their attacks of angina pectoris.

A factor present in all cases of essential hypertension is increased cardiac work;* this has been shown to be of importance in the angina pectoris associated with thyrotoxicosis, and perhaps in chronic anemia. It is probably important in the production of angina pectoris in cases of hypertension without severe coronary disease. For example, in Cases 4, 5, and 6 the cardiac hypertrophy was slight, and the angina pectoris was probably related to the increased work.

Thus there are two factors present in patients with hypertension whose angina pectoris is associated with lesser degrees of coronary sclerosis: (1) cardiac hypertrophy and (2) increased cardiac work.

SUMMARY AND CONCLUSIONS

1. The anatomic findings in forty cases of angina pectoris with hypertension and twenty-one cases of angina pectoris without hypertension were compared.

*Cardiac work = cardiac output × mean blood pressure.[11]

2. An extreme degree of coronary disease, involving two or more major arteries, was present in 95 per cent of the patients without hypertension, and in only 39 per cent of the patients with hypertension.

3. The incidence of myocardial infarction was correspondingly very much higher in the patients without hypertension.

4. Angina pectoris thus often develops with less coronary disease if the patient has hypertension.

5. Factors other than coronary insufficiency, which are important in the production of angina pectoris in hypertensive heart disease, are (1) cardiac hypertrophy and (2) increased cardiac work.

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ELECTROCARDIOGRAPHIC OBSERVATIONS ON PNEUMOPERITONEUM*

BENJAMIN J. ELWOOD, M.D., GEORGE F. PILTZ, M.D., AND
BENJAMIN P. POTTER, M.D.
JERSEY CITY, N. J.

THE importance of electrocardiography in cases of pulmonary tuberculosis is that associated myocardial disease or conduction disturbances are occasionally disclosed. That pulmonary tuberculosis itself does not produce much modification of the electrical complexes, except, occasionally, for low voltage in Lead I or Leads I and II,[1, 2] is generally recognized. Furthermore, axis deviation secondary to displacement of the heart by pleural effusion, adhesions, or collapse therapy may not be demonstrated with uniformity.[3, 4, 5] Nevertheless, there is abundant evidence[6, 7, 8, 9, 10, 11, 12, 13] that changes in the electrical axis and T wave occur with experimental shifting and rotation of the heart in a number of cardiac derangements and when the heart is normal in cases of obesity and pregnancy. The latter two conditions produce a definite change in the physical habitus of the individual and, manifestly, in the position of the diaphragm, so that the anatomic axis of the heart is altered. Pneumoperitoneum therefore appeared to offer a suitable opportunity for making further observations of these phenomena.

As has been shown by a number of investigators,[14, 15, 16] pneumoperitoneum produces an elevation of the diaphragm and, probably by favoring relaxation of the pulmonary parenchyma, promotes healing of infiltration and closure of cavities. This beneficial effect upon tuberculous disease is not unlike that noted after phrenicectomy and, at times, during the course of a complicating pregnancy. The extent of artificial upward displacement of the diaphragm can be varied with each subject, and otherwise depends upon the amount of air in the peritoneal cavity. Any changes, therefore, in the position of the heart are obviously in proportion to the amount of elevation of the diaphragm, particularly the left side, upon which the heart largely rests. Radiographic and fluoroscopic observations disclosed that as the diaphragm rose the heart assumed a more transverse position and rotated slightly. The more complete details of these anatomic relationships were brought out in postmortem specimens, and pertinent observations will be correlated below.

Twenty patients with pulmonary tuberculosis were selected for pneumoperitoneum therapy and were examined electrocardiographically

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From the Hudson County Tuberculosis Hospital, Jersey City, N. J., Dr. B. S. Pollak, Medical Director.
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during the course of treatment. In ten cases a comparison could be made with electrocardiograms obtained before the institution of therapy, and, in fifteen, tracings were correlated after complete resorption of air from the peritoneal cavity. Additional observations may be offered

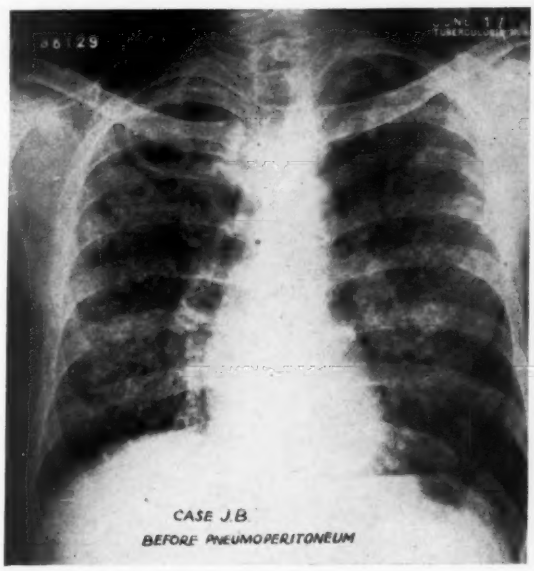

Fig. 1.—Case J. B. Before pneumoperitoneum.

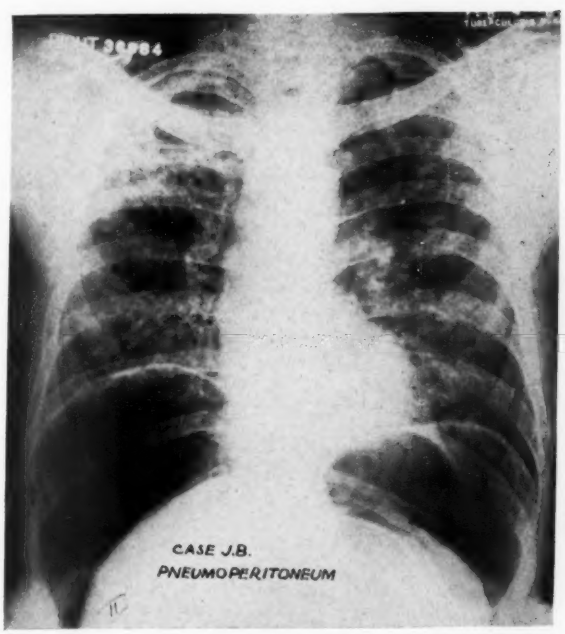

Fig. 2.—Case J. B. After pneumoperitoneum. Note change in position of diaphragm and alteration in position and shape of heart.

on six patients who underwent phrenic nerve operations which selectively supplemented the elevation of one-half of the diaphragm or ultimately replaced the pneumoperitoneum treatment. The efficacy of the treatment need not be evaluated here.

THE ELECTROCARDIOGRAM BEFORE PNEUMOPERITONEUM WAS PRODUCED

In the ten cases in this group the electrocardiograms were essentially normal. No instance of axis deviation was noted, and low voltage in

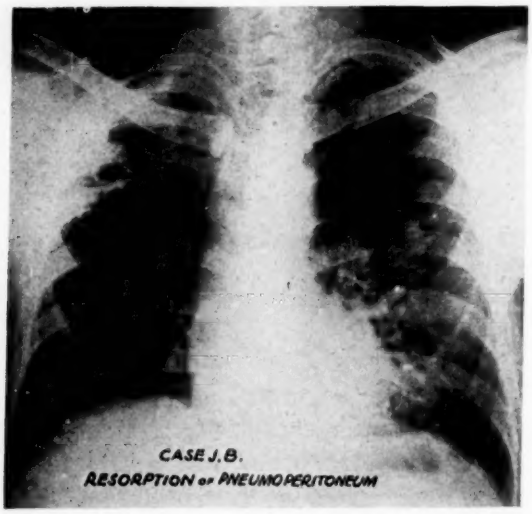

Fig. 3.—Case J. B. After pneumoperitoneum completely resorbed. Note return of diaphragm to normal level and restoration of heart to original position and shape.

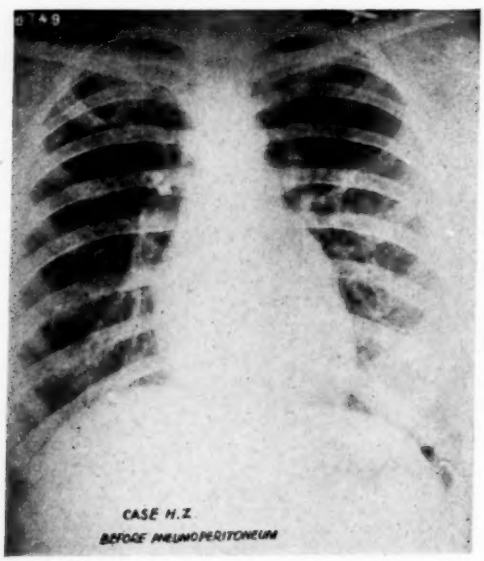

Fig. 4.—Case H. Z. Before pneumoperitoneum.

Lead I or Leads I and II was not encountered. The T wave in Lead III was inverted in two, and isoelectric in two others. The tuberculosis was moderately to far advanced in all, and there was no unusual disproportion in the levels of the hemidiaphragms or deviation of the

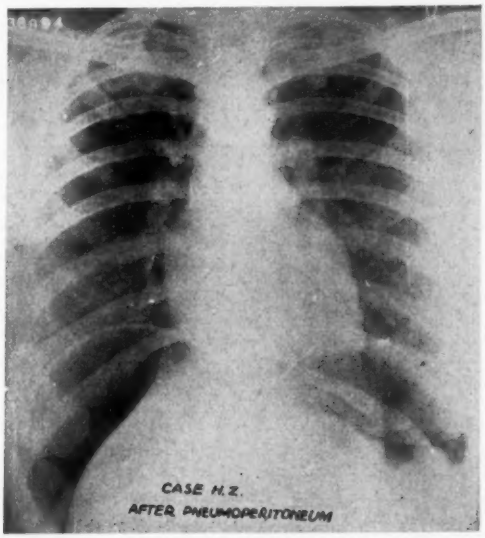

Fig. 5.—Case H. Z. After pneumoperitoneum.

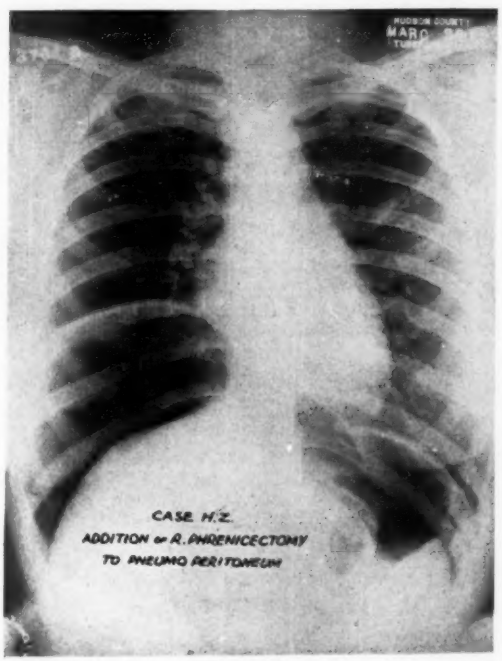

Fig. 6.—Case H. Z. Note effect of adding phrenicectomy (with further elevation of right hemidiaphragm) on position of heart.

cardiac structures to one or the other side. All patients, with the exception of three who were over 40 years of age, were young adults; none disclosed any evidence of cardiac disease.

THE ELECTROCARDIOGRAPHIC CHANGES PRODUCED BY PNEUMOPERITONEUM

Alterations (Table I) were noted chiefly in R_1 and the Q, R, and T waves of Lead III. Other components of the electrocardiogram exhibited too few and inconstant changes to merit discussion.

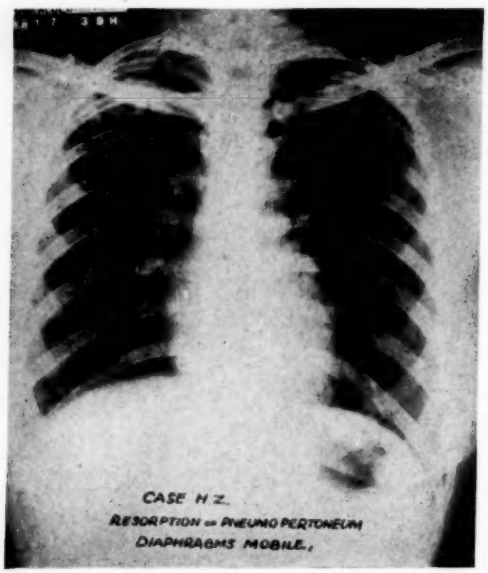

Fig. 7.—Case H. Z. After complete resorption of pneumoperitoneum and return of function of diaphragm. Compare shape and position of hearts before and after therapeutic procedures.

TABLE I

ELECTROCARDIOGRAPHIC CHANGES PRODUCED BY PNEUMOPERITONEUM

ECG FINDINGS BEFORE PNP.		ECG CHANGES WITH PNP.	
No. of Cases	10	No. of Cases	10
R_1 Upright	10	R_1 Amp. Incr.	10
R_3 Upright	10	R_3 Amp. Decr.	8
R_3 Inverted	0	R_3 Inverted	2
Deep Q_3	0	Deep Q_3	4
T_3 Isoelect.	2	T_3 Isoelect.	1
T_3 Inverted	2	T_3 Inverted	9
		L. Axis Dev.	10
Axis Deviation	0	L. Axis Dev.	6

Additional observations in 10 other cases in which no electrocardiogram was made before pneumoperitoneum: R_1 amp. increased, R_3 amp. decreased, when pnp. increased; R_3 inv. 1, deep Q_3 2, T_3 inv. 8, L.A.D. 3.

Changes in the QRS Complex.—Without exception, the production of pneumoperitoneum in the ten patients mentioned above was followed by a definite deviation of the electrical axis to the left, marked by an in-

crease in the amplitude of R_1 and a decrease in the amplitude of R_3, with inversion of the latter in two instances, and the development of a prominent Q_3 in four instances.

Left axis deviation was complete in six. When the maximum degree of pneumoperitoneum was obtained, no further deviation of the axis could be demonstrated. The remaining ten patients were first examined electrocardiographically after pneumoperitoneum had been well established. Nevertheless, serial curves taken with increasing degrees of pneumoperitoneum revealed uniform shifting to the left. In addition, two more instances of a deep Q_3, two of left axis deviation, and one of a variably high S-T takeoff in Lead III were encountered.

Changes in the T Wave in Lead III.—Inversion of T_3 was found in two out of ten cases before pneumoperitoneum was established. Of the remaining eight cases, the induction of pneumoperitoneum caused the T wave to become negative in 7, and isoelectric in one. Of the ten cases in which electrocardiograms were not made until pneumoperitoneum was already established, T-wave inversion in Lead III was encountered in eight. The close similarity of the changes in this latter group to those in the former would lead to the belief that pneumoperitoneum was the cause.

TABLE II

PHRENICECTOMY IN ADDITION TO PNEUMOPERITONEUM

CASE	1	2	3	4	5	6
R or L	R	R	R	R	L	L
Diaphr. Rise	Yes	Yes	Yes	Yes	No	Yes
R_1 Amplitude	Decr.	Decr.	Decr.	Decr.	N.C.	Incr.
R_3 Amplitude	Incr.	Incr.	Incr.	Incr.	N.C.	Decr.
Q_3 Depth	Decr.	0	Decr.	Decr.	N.C.	Incr.
T_3	Upr.	Upr.	Inv.	Inv.	Inv.	Inv.
T_3 with Pnp.	Inv.	Inv.	Inv.	Inv.	Inv.	Inv.
T_3 Before Pnp.	Upr.	Upr.	Inv.	Inv.	Upr.	Inv.
Axis Deviation	R.	R.	R.	R.	N.C.	L.

THE EFFECT ON THE ELECTROCARDIOGRAM OF ADDING PHRENICECTOMY TO PNEUMOPERITONEUM

The electrocardiographic changes are listed in Table II. It is clear that phrenicectomy, producing a further rise of the right hemidiaphragm, is accompanied by a deviation of the electrical axis to the right, with a loss or lessening of any left axis deviation which may have been present previously. When left-sided phrenicectomy caused a further rise of the left side of the diaphragm, the electrical axis was deviated still more to the left, but when cutting the nerve caused no additional elevation of the diaphragm, the electrocardiogram remained unchanged. T waves in Lead III which had been inverted by pneumoperitoneum became upright after right-sided phrenicectomy. Left-sided phrenicectomy had no effect on T-wave inversion in Lead III.

THE ELECTROCARDIOGRAM DURING AND AFTER RESORPTION OF AIR FROM THE PERITONEAL CAVITY

Fifteen patients were followed through the stage of resorption of air from the peritoneal cavity, until the diaphragm returned to its original level. The accompanying electrocardiographic changes are shown in Table III.

TABLE III

ELECTROCARDIOGRAPHIC CHANGES WITH RESORPTION OF AIR FROM PERITONEAL CAVITY IN 15 CASES

R_1			Decreased	12
			No Change	3
R_3			Increased	12
			No Change	3
Q_3	Deep	6	Less Prom.	1
			Absent	5
	Inv.	12		
T_3	Flat	1	Inverted	3
	Upr.	2	Upright	12

It is to be noted that in twelve of fifteen cases deviation of the electrical axis to the right occurred, with complete restoration of the original (normal) axis. The deep Q wave in Lead III which developed in four cases during pneumoperitoneum disappeared in every instance; it disappeared in one of the two cases of previously established pneumoperitoneum and became less prominent in the other.

In nine of ten instances in which T_3 had been rendered negative by pneumoperitoneum, it became positive again. In three it remained inverted; in two of these the inversion was present before and during pneumoperitoneum therapy, and in the third the inversion was less pronounced. In the three remaining cases the T waves in Lead III, which had been positive or isoelectric when pneumoperitoneum was present, increased in amplitude.

These observations indicated clearly that the original electrical and anatomic axes of the heart were restored after the air was resorbed. With the return of the diaphragm to its original position, there was a deviation of the electrical axis to the right, and parallel changes occurred in the amplitude and direction of T and R in Lead III. Why elevation of the right side of the diaphragm subsequent to phrenicectomy results in changes comparable to those noted when both sides of the diaphragm return to the normal position, and why elevation of the left side of the diaphragm alone produces alterations such as those caused by pneumoperitoneum remain to be explained. Access to fresh post-mortem material furnished the evidence that the position of the left side of the diaphragm in relation to the right accounts largely for the direction of the anatomic axis of the normal heart.

After the sternal plate had been carefully removed, a window was cut in the pericardium to expose the heart, which was seen to lie almost entirely on the left side of the diaphragm, in the anterior costophrenic

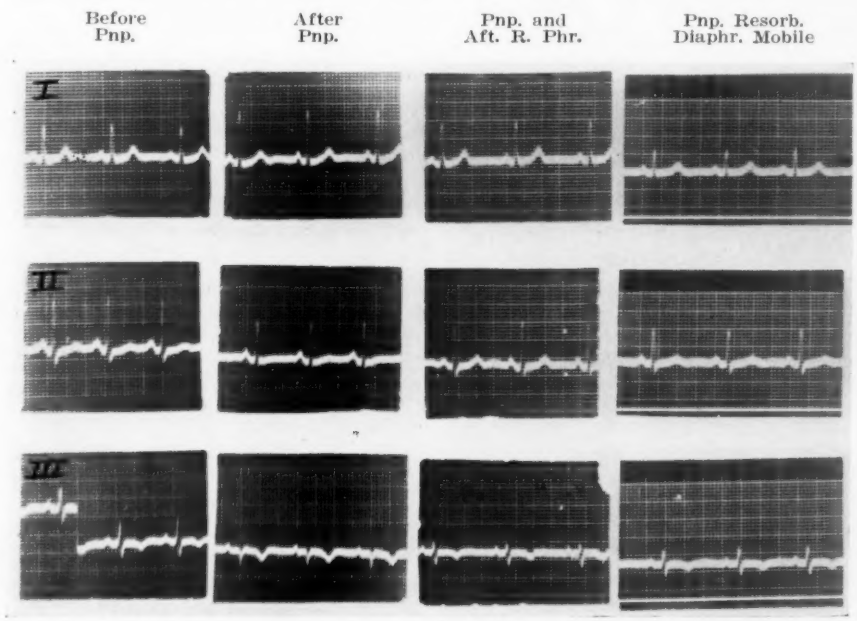

Fig. 8.—Composite electrocardiogram (one case) showing various changes occurring with alteration of position of one or both halves of the diaghragm.

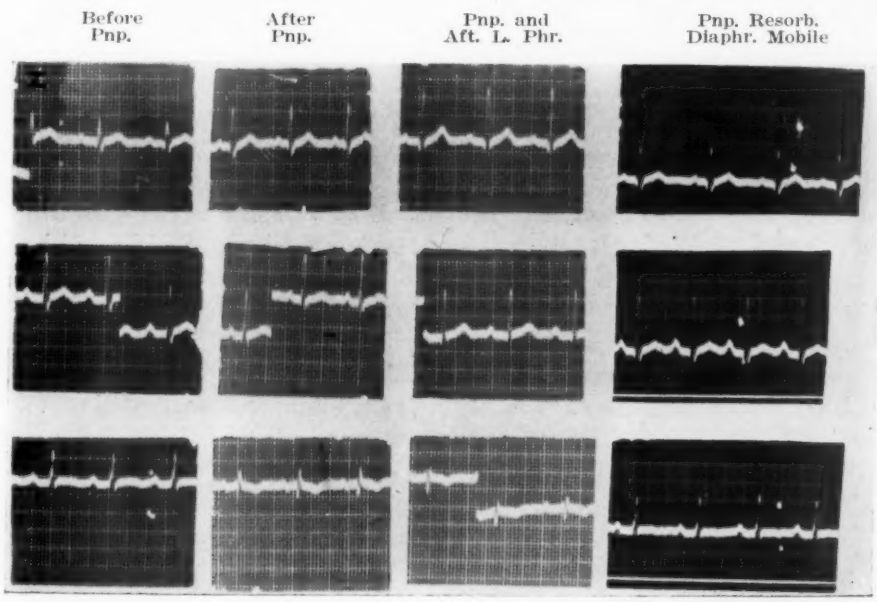

Fig. 9.—Composite electrocardiogram (one case) showing various changes occurring with alteration of position of one or both halves of the diaphragm.

sulcus. Thus, anatomic relationships clearly governed cardiophrenic dynamics. Displacement upward of the left side of the diaphragm, either alone or in conjunction with displacement of the right, causes the heart to assume a more transverse position; the apex rotates counterclockwise on its anteroposterior axis, and, at the same time, the heart rotates in a slight clockwise manner on its longitudinal axis. The opposite effects are produced as the left or both hemidiaphragms are allowed to return to their original position. When the right side of the diaphragm alone is displaced upward, the alteration in the anatomic axis is caused by a slight tipping upward and forward of the right border of the heart, while the apex rotates downward and slightly backward. This behavior, although less marked, is the direct opposite of that observed when the left or both hemidiaphragms are elevated, and definitely lends the impression that the relative position of the left hemidiaphragm has a dominating effect upon the anatomic axis. The electrical aspect of this effect is clearly portrayed in the electrocardiogram. Similar changes in the electrical axis and T wave occur when both hemidiaphragms, or the left alone, are elevated, and when the right hemidiaphragm rises and the left or both are caused to return to normal position.

DISCUSSION

The correlation of changes in the anatomic and electrical axes has been the subject of frequent study. It is generally recognized that when the anatomic axis is altered, the electrocardiogram does not necessarily show any change in the path of the excitation wave. The extent to which the position of the diaphragm determines the location of both the anatomic and electrical axes of the heart may be shown in studies on pneumoperitoneum. Einthoven,[17] et al., demonstrated that deep breathing affects the form of the electrocardiogram, and that the end of expiration is associated with a tendency to left axis deviation. Carter[18] further states that any change in the position of the heart causes left axis deviation more often than right axis deviation. The relative ease with which the amplitude and direction of the R wave in Lead III could be altered, in contrast to the difficulty of changing R_1, by producing pneumoperitoneum would tend to bear out the latter opinion. The deviation in the axis when the hemidiaphragms are in a normal position may be betrayed only by low voltage in Lead I, particularly of the QRS complex. What has been noted previously in pulmonary tuberculosis as a variable finding, namely, low voltage in Lead I or Leads I and II, now takes on added significance, and is probably caused by the relatively low position of the diaphragm in a certain number of instances. That a high diaphragm tends to displace the electrical axis to the left is supported by studies on obesity[19, 20, 21] and pregnancy,[22, 23, 24, 25, 26] and that deviation to the right occurs when these conditions are removed has also been shown.

The association of a deep Q wave in Lead III with coronary disease, and its rare occurrence in normal hearts, have been pointed out by Pardee[27] and confirmed by Willius,[28] Fenichel and Kugel,[29] and others. Its relatively frequent development in pregnancy has been demonstrated by Carr, Hamilton, and Palmer,[30] who suggest that such a deep Q may be related to a transverse position of the heart. Leverton,[31] in an extended analysis of electrocardiograms of tuberculous patients, encountered twelve instances in which there was a prominent Q_3 without any obvious reason; in five of these cases the left hemidiaphragm was high, and two of the patients were obese. The question was therefore raised as to the influence of change in the position of the heart upon the occurrence of Q waves, especially in those patients who had elevation of the diaphragm. The occurrence of a deep Q in six of twenty cases (30 per cent) in which the diaphragm was elevated by pneumoperitoneum would tend to confirm the interpretation of Carr, et al., and Leverton.

Studies[13, 21, 25, 32] have been made of the behavior of the T wave in association with axis changes, with or without myocardial disease. Clinical evidence indicates that in the absence of a low or inverted T in Lead I and an erect T in Lead III, left axis deviation is not indicative of heart disease. On the other hand, when a change in the axis is a result of a change in the position of the heart, the QRS and T waves in Leads I and III tend to behave uniformly. The frequency with which inversion of T in Lead III was associated with left axis deviation in the presence of pneumoperitoneum clearly supports these observations, and constitutes further evidence of the significance of these findings in cases of obesity and pregnancy in which the heart is normal.

It is curious to note that Hoffman[33] and Grau[34] observed that insufflation of the stomach produces an increase in the amplitude of R and T in Lead I, and converse changes in Lead III, which are essentially the same alterations as those maintained or accentuated by elevation of the left half of the diaphragm secondary to phrenicectomy. Although electrocardiographic studies of patients after phrenicectomy[35-38] have yielded similar findings only occasionally, more detailed studies appear to be indicated, especially in view of the constant effects, as shown at autopsy, which the position of the individual hemidiaphragms produces upon the anatomic axis of the heart.

SUMMARY AND CONCLUSIONS

1. The electrocardiographic changes produced by pneumoperitoneum in twenty cases of pulmonary tuberculosis are analyzed.

2. The effect of the position of the diaphragm on the anatomic axis of the heart has its counterpart in a deviation of the electrical axis. Elevation of both hemidiaphragms or of the left hemidiaphragm alone results in left axis deviation and inversion of the T wave in Lead III.

The opposite effect is produced when the position of both hemidiaphragms, or of the left alone, returns to normal. The action of the right side of the diaphragm counteracts that of the left, but the latter dominates, and is the chief factor in altering the position of the heart and producing the electrocardiographic changes.

3. Low voltage in Lead I or Leads I and II, which has been reported as a characteristic occurrence in a variable number of cases of pulmonary tuberculosis, is probably an indication of right axis deviation caused by low position of the diaphragm.

4. A high position of the diaphragm may produce a relatively high incidence of deep Q waves in Lead III.

5. The T wave in Lead III tends to behave in the same way as the QRS complex when axis deviation is a result of alteration in the anatomic position of the heart.

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THE EFFECT OF CHRONIC CONSTRICTION OF THE AORTA ON ARTERIAL BLOOD PRESSURE IN DOGS: AN ATTEMPT TO PRODUCE COARCTATION OF THE AORTA

IRVINE H. PAGE, M.D.
INDIANAPOLIS, IND.

THOROUGH anatomic studies have established the fact that the occurrence of signs and symptoms of the adult type of coaretation of the aorta depends upon the efficacy of the collateral blood supply to the lower extremities, rather than upon the degree of obstruction (Hamilton and Abbott,[1] 1927-28). Large collateral vessels develop chiefly between the superior intercostal artery, which arises from the subclavian artery above the constriction, and the first and second intercostal arteries just below the constriction. Indeed, so great is the influx of returned blood at this point that aneurysmal dilatation of the aorta often occurs (Abbott,[2] 1927-28).

Studies of the dynamics of the circulation in aortic coaretation have been few, and limited to small numbers of patients. Our knowledge of cardiac output, for example, appears to rest on the results of examination of but one patient by Grollman and Ferrigan[3] (1934), in whom it was found to be normal. The pulse waves in the femoral vessels are retarded, chiefly because of the greater time required for blood to pass through the collateral circulation. The blood flow to the extremities has been found to be normal by Lewis[4] (1933), Blumgart, Lawrence, and Ernstene[5] (1931), and Pickering[6] (1936), and below normal in the arms by Prinzmetal and Wilson[7] (1936).

Arterial blood pressure may be higher in the upper extremities than in the lower when the stenosis is of marked degree, but coaretation sufficient to produce characteristic physical signs and a difference of pressure between arms and legs may exist in an adult with normal brachial blood pressure (King,[8] 1937). The only direct measurement of intra-arterial pressure, employing a recording device for both systolic and diastolic pressure, is that made on one patient by Steele and Cohn[9] (1938). They found that the pulse pressure in a femoral vessel was very low (11 to 15 mm. Hg), and the diastolic pressure nearly as high as in the arms, i.e., 108 to 120 mm., as contrasted with 120 to 130 mm. Hg. The systolic pressures were 120 to 130 mm. in a femoral artery and 180 to 192 mm. Hg in a radial vessel. Steele[10] (1939) has further shown that clamping the aorta near the orifices of the renal arteries in dogs is followed by elevation of the diastolic pressure in the hind legs as well as in the carotid arteries, indicating a widespread increase in peripheral resistance.

Lilly Laboratory for Clinical Research, Indianapolis City Hospital.
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It is agreed that the blood flow in the arms is not *increased*, and, since the arterial pressure is elevated, hypertonus must be present. The same reasoning may apply to the legs. Sharp disagreement exists as to the cause of the hypertonus. Prinzmetal and Wilson[7] (1936) found that the increase of blood flow resulting from application of heat to the opposite arm was much greater in patients with coarctation than in normal persons. They concluded that the hypertonus was of vasomotor origin. On the contrary, Pickering[6] (1936) did not observe any abnormal response to heat. He writes, "A chemical abnormality of the blood is clearly out of the question and it was anticipated in this condition that the vascular narrowing would be found to be of nervous origin, although no appropriate reflex nervous mechanism is known which would produce increased vascular tone restricted to the upper half of the body." He therefore attributed the vascular narrowing to local change in the vessels.

Blumgart, Lawrence, and Ernstene[5] (1931) do not believe that hypertonus exists in the arterioles because they found that the arteriolar blood pressure in the arms of two patients with coarctation was normal. They suggested that the increased peripheral resistance is caused, not by increased arteriolar resistance, but rather by the resistance offered by the constricted aorta and the collateral pathways.

Thus, there are three conflicting explanations, the one that hypertonus is of nervous origin, another that it is caused by intrinsic fault in the vessels, and a third that hypertonus is not present and that peripheral resistance is increased only by the constricted aorta and collateral circulation. A fourth possibility, namely, that it results from a chemical abnormality of the blood, has been discarded on what appears to be insufficient evidence.

The suggestion was made by several investigators, including Page[11] (1937), Goldblatt and Kahn[12] (1938), and Rytand[13] (1938), that coarctation might be reproduced in dogs by clamping the aorta, as Goldblatt, Lynch, Hanzal, and Summerville[14] (1934) had done to the renal artery. Goldblatt and Kahn[12] (1938), in a preliminary communication, and Goldblatt, Kahn, and Hanzal[15] (1939) reported the production of hypertension in dogs by chronic constriction of the abdominal aorta just above the site of origin of the renal arteries.

Rytand[16] (1938) found in rats that cardiac hypertrophy follows partial occlusion of the aorta near the mouths of the renal vessels. He concluded that, if the cardiac hypertrophy was caused by hypertension, the hypertension was produced by the same mechanism as that following clamping of the renal vessels, and that the hypertension of coarctation had a similar origin. As both Goldblatt and Kahn, and Rytand, constricted the aorta close to the origin of the renal vessels, it is probable that the hypertension which resulted did not differ in origin from that caused by constriction of the renal vessels themselves, but the suggestion of Rytand that coarctation of the aorta of the adult type had been re-

produced does not appear justified, for the occlusion in human coarctation is close to the heart and not near the renal vessels.

We have attempted to reproduce the hemodynamic disturbances which occur in coarctation by clamping the aorta at various levels in dogs, in order to learn something of the mechanism of the hypertension which results when the proper level is constricted.

METHOD

Compression of the aortae of dogs was achieved by means of large stainless-steel clamps made on the same principle as those of Goldblatt, Lynch, Hanzal, and Summerville[14] (1934). Under intratracheal ether anesthesia the thorax was entered and, after dissecting free a portion of aorta, the clamp was applied so that it fitted snugly on the aorta but did not compress it. The clamp was removed and the width of the aorta measured with calipers by measuring the distance between the fixed and the movable plates of the clamp. It was then reapplied, and tightened until the arterial pressure in the femoral artery fell to the desired level. The head of the screw in the clamp was buried in the dorsal musculature, the lungs reflated, and the thorax closed. At autopsy the extent of the constriction was ascertained. A number of variations in the procedure of applying the clamp were employed. (1) In certain experiments one kidney was removed and the other transplanted under the skin. (2) In others the kidneys were wrapped in cellophane to prevent development of collateral circulation. (3) In order to secure more complete occlusion of the aorta, some animals were prepared in the following manner. First, one kidney was removed and the abdominal aorta occluded about 4 cm. below the origin of the renal vessels. In most cases, disturbance of the circulation to the legs was not sufficient to interfere with the animal's walking, but, if the legs were paralyzed, the clamp was partially opened and the next day closed again. Second, from two to seven days later, the thoracic aorta was clamped. The closer the clamp on the aorta was to the heart, the greater was the danger of causing death, either from cardiac failure within an hour or two after the operation, or because the clamp would cut through the aorta within a few days. (4) These difficulties were to some extent overcome by clamping the aorta in two or more stages. A clamp was placed (usually on the horizontal portion of the arch) and adjusted to constrict the vessel to about one-half its normal diameter. A week later the thorax was again entered, and a second clamp placed 2 cm. below the first and closed as far as desired. (5) In two experiments cellophane or silk was wrapped around the aorta at the initial operation, and three weeks later the clamp was applied to this area. Scar tissue which had formed around the aorta appeared to help prevent the clamp from cutting through the aorta (Fig. 1).

Blood pressure measurements were made by intra-arterial puncture with a 20-gauge needle. At the first operation both carotid arteries were transplanted under the skin and the femoral arteries were dissected free to increase the ease with which they could be reached with the needle. The needle was connected to a mercury manometer by means of rubber tubing filled with heparin solution. If the arterial pressure or heart rate was widely variable before operation, the animal was discarded.

RESULTS

Our first experiments were, as we discovered later, largely a repetition of those of Barcroft[17, 18] (1931-34). Acute occlusion of the thoracic aorta with the animal anesthetized produced a sharp rise in blood pressure in

the carotid artery. The rise occurred even after the animal had been pithed, the kidneys and adrenals removed, and the abdomen eviscerated.

Of interest is the fact that this temporary rise occurs only when the aorta is occluded proximal to the origin of the renal vessels. Compression of the aorta below this region produces slight, if any, rise of intracarotid pressure. Presumably this is because of the fact that the mesenteric vessels are not closed when the aorta is compressed below the origin of the renal vessels.

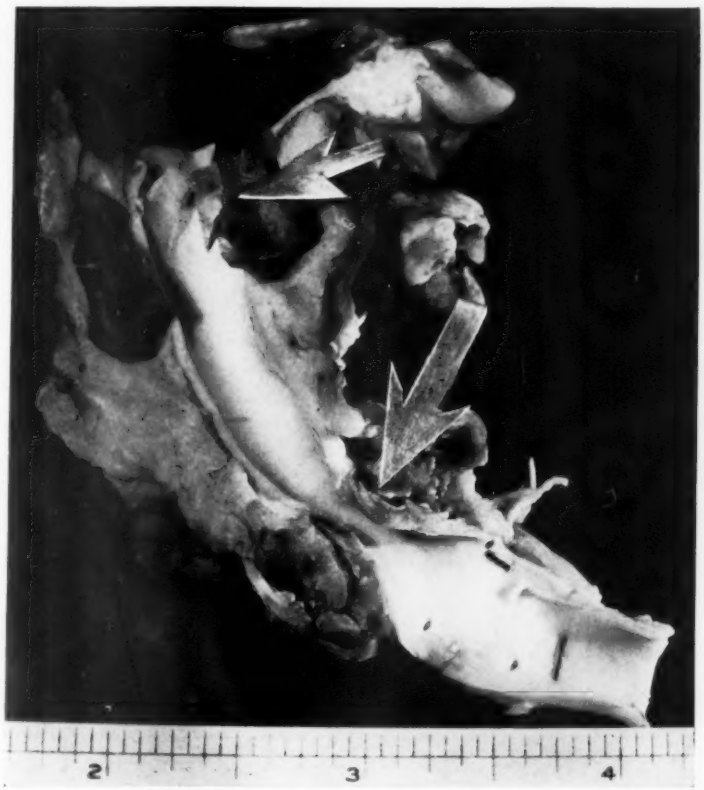

Fig. 1.—Experiment illustrating the return toward normal of pressure in the femoral artery, without corresponding rise of carotid pressure, after clamping the aorta in the thorax. Upper tracing represents femoral pressure and lower intracarotid pressure. Animal was anesthetized with paraldehyde. The sections of the graph were taken twenty minutes apart. (Time intervals, six seconds.)

Effect on Arterial Blood Pressure of Clamping the Aorta Low in the Thorax.—Both normal and uninephrectomized dogs were employed for this operation, as it has been the experience of many investigators that hypertension is produced more readily by clamping the renal artery of dogs in which one kidney has been removed. A third group of animals were used, in which, after uninephrectomy, the remaining kidney was transplanted under the skin, so that at a later time the kidney could be easily removed. The clamp on the aorta was placed about 2 to 4 cm.

TABLE I

EFFECT ON CAROTID AND FEMORAL ARTERIAL PRESSURE OF UNINEPHRECTOMIZED AND NORMAL DOGS OF CLAMPING THE AORTA LOW IN THE THORAX, FOLLOWED IN SOME CASES BY NEPHRECTOMY

DOG NO.	NATURE OF OPERATION	INTRA-ARTERIAL BLOOD PRESSURE MM. HG				
		BEFORE OPER.	AFTER OPERATION OF CLAMPING AORTA			
		FEMORAL B. P. MM. HG	TIME (IN HOURS)	CAROTID (B. P. MM. HG)	FEMORAL (B. P. MM. HG)	PULSE RATE
1	Uninephrec.	110	3	120	90	152
		116	6	130	–	–
		120	22	134	94	104
				Clamp tightened		
			6	150	40	120
			18	134	–	155
				Kidney removed		
			20	120	–	160
2	Uninephrec.	122	2	160	96	160
		116	2¾	166	–	140
		130		Kidney removed		
			4	137	94	68
			5	150	–	100
			11	153	96	104
			24	98	32	84
3	Uninephrec.	130	2	144	64	176
		110		Kidney removed		
		124	3½	112	71	104
			24	116	62	124
			48	116	56	58
4	Uninephrec.	122	3	136	46	
		118		Kidney removed		
			5	112	34	
			6	134	44	
5	Uninephrec.	124	3	154	110	
		130		Kidney removed		
			5½	140	114	
			23	114	114	
			48	114	114	
6	Uninephrec.	126	2½	110	84	
				Kidney removed		
			4½	134	78	
7	Uninephrec.	120	½	126	72	
			3	154	68	
				Kidney removed		
			4½	124	64	
			6	98	74	
8	Uninephrec.	148	48	168	60	
		102				
		154				
		160				
9	Uninephrec.	122	2	138	8	200
		120				
10	Normal	120	¼	–	30	–
		126	3½	155	92	156
			5½	137	94	100
			24	140	64	84
			48	136	86	90
			72	134	–	128

TABLE I—CONT'D

DOG NO.	NATURE OF OPERATION	INTRA-ARTERIAL BLOOD PRESSURE MM. HG				
		BEFORE OPER.	AFTER OPERATION OF CLAMPING AORTA			
		FEMORAL B. P. MM. HG	TIME (IN HOURS)	CAROTID (B. P. MM. HG)	FEMORAL (B. P. MM. HG)	PULSE RATE
11	Normal	90	5	134	90	116
		132	22	132	90	72
		114	48	140	86	130
			72	167	110	132
	Almost moribund		144	94	–	90
12	Normal	132	¼	170	26	160
		150				
		146				
		132				
13	Both kidneys in cellophane	130	5	130	83	80
		131	24	130	86	80
		124	48	141	49	74
		120	72	150	112	84
		138	120	150	70	80

below the dome of the diaphragm, and the lumen of the vessel almost closed (3 to 18 per cent patent). At autopsy in a few of the animals the lumen was found to be completely obliterated.

From one to four hours after operation the arterial blood pressure was slightly higher than the normal of 120 to 150 mm. Hg (Table I); the maximum was 170 mm. Hg, and the average, 150 to 160 mm. Hg. If the remaining kidney was removed under local anesthesia during the first two to three hours, the blood pressure returned to normal. However, even without nephrectomy, the arterial pressure tended to fall after the first six hours. The femoral blood pressure often rose rapidly within the first hour after clamping (Fig. 2), and then remained moderately stable. Pressures as low as 8 and 26 mm. Hg were observed, but the majority were 60 mm., or more.

The size of the remaining lumen varied usually from about 3 to 18 per cent of the original, as calculated from the formula of Gibbon, Hopkinson, and Churchill[19] (1932), namely, $O = \pi r\ (2R - r)$, in which O represents the area of cross section of the artery, R, the original internal radius of the artery, and r, one-half of the difference between 2R and the distance which the movable plate of the clamp has moved toward the fixed plate. For example, in Dog 16 the area of the cross section of the normal aorta was 22.3 sq. mm., and, after compression, it was 1.55 sq. mm., or 6.9 per cent of the original. Our results for the aorta are similar to those of Gibbon, Hopkinson, and Churchill[19] (1932) for the pulmonary artery in demonstrating the severity of the compression necessary before volume flow is seriously reduced. Almost no reduction in pressure occurs until from 65 to 80 per cent of the original cross section of the artery is obliterated. The fall in pressure is very sharp after the critical point in the reduction of the cross-sectional area is reached. These results

corroborate those of Mann, Herrick, Essex, and Baldes[20] (1938), which were published after completion of this work.

Examination of the vessels within the clamp after sectioning and staining showed that moderate necrosis of the vessel wall had occurred, and, in some, there were marked thinning and stretching. After a period of time, more blood must flow through the clamped portion of the vessel because of this thinning of its walls.

Effect of Clamping the Aorta Both Below the Kidneys and Low in the Thorax.—At the initial operation a clamp was placed on the aorta about 4 cm. below the origin of the renal vessels, and closed. After three to five days another clamp was placed on the aorta low in the thorax, but not completely closed (about 20 per cent of the lumen remained open).

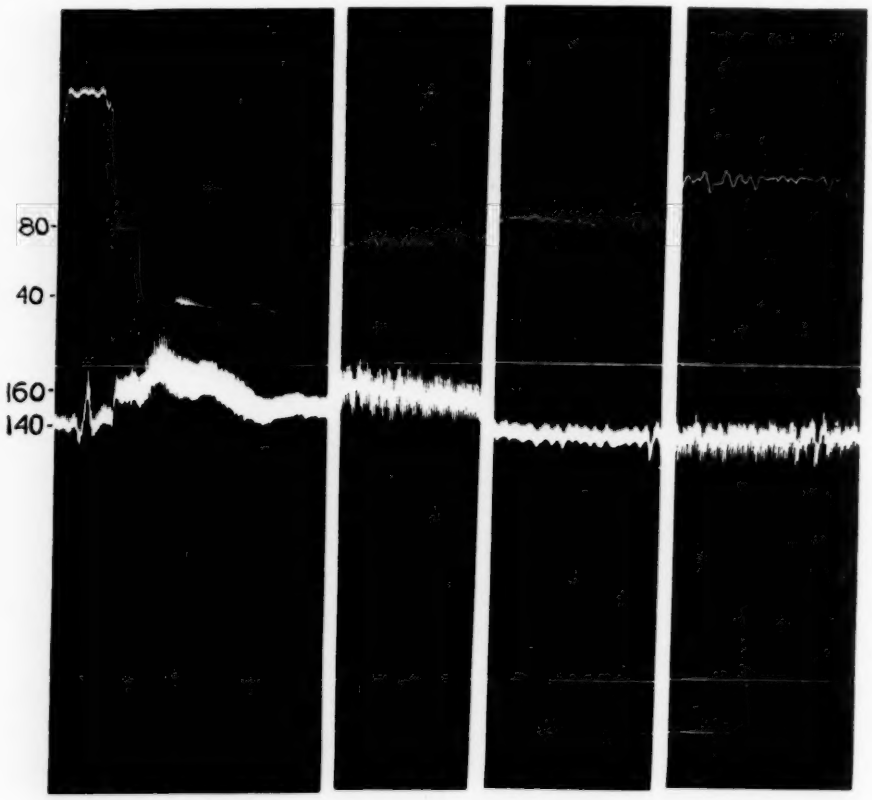

Fig. 2.—Re-enforcement of the aorta by application of cellophane, followed by application of a metal clamp below the re-enforced area. The upper arrow points to the arch of the aorta and to portions of cellophane surrounded by thick supporting tissue, which extends down to the second arrow where the aorta was closed by the clamp.

When the aorta was occluded below the kidneys, no rise in blood pressure occurred (Table II, Dogs No. 14 to 19), and no greater fall in femoral pressure was observed than when the aorta was clamped in the lower thorax. If, now, a second clamp was placed on the aorta in the lower thorax of the animals in which the aorta was clamped below the

TABLE II

EFFECT ON CAROTID AND FEMORAL ARTERIAL PRESSURE OF CLAMPING THE AORTA BELOW THE KIDNEYS, COMBINED WITH CLAMPING THE THORACIC AORTA FOLLOWED LATER BY NEPHRECTOMY

	INTRA-ARTERIAL BLOOD PRESSURE MM. HG				
	BEFORE OPER.	AFTER OPERATION OF CLAMPING AORTA			
DOG. NO.	FEMORAL B. P. MM. HG	TIME (IN HOURS)	CAROTID (B. P. MM. HG)	FEMORAL (B. P. MM. HG)	PULSE RATE
14		Normal Dog, Clamp Below Kidneys			
	144	5	148	123	68
	140	22	174	138	52
	124	46	156	136	62
	146	70	144	111	72
	130	166	162	130	58
		262	132	70	94
		406	142	107	72
15		Normal Dog, Clamp Below Kidneys			
	133	24	132	108	108
	154	62	133	120	82
	138	254	118	74	72
	140	326	158	90	120
16		Normal Dog, Clamp Below Kidneys			
	123	½	151	100	150
	140	20	136	78	58
	142	47	146	71	88
	144	167	146	79	70
17		Normal Dog, Clamp Below Kidneys			
	134	¼	126	86	162
	142	25	125	62	104
	140	49	136	64	92
	132	121	153	90	92
		337	140	61	80
18		Clamp Closed 3 cm. Below Kidneys			
	136	24	132	56	92
	148				
	139	72	130	89	146
19		Left-sided Nephrectomy + Abdominal Aorta Clamp			
	122	72	138	102	108
	116				
	124				
20		Aorta Clamp Closed 4 cm. Below Renal Vessels			
	120	30	136	56	100
	118	144	144	94	98
	124	Aorta Clamped Just Above Crura of Diaphragm			
		168	170	90	72
		192	184	105	98
		240	190	100	78
21	132	Uninephrectomy and Abdominal Aorta Clamped			
	120	Aorta Clamped at Level of Dome of Diaphragm			
	130	72	146	61	78
	138	96	154	62	70
		120	202	28	48
		Remaining Kidney Removed			
		123	78	0	90
		Urea Nitrogen 126.5 mg. for 100 c.c., 6 hours later			

TABLE II—CONT'D

DOG. NO.	INTRA-ARTERIAL BLOOD PRESSURE MM. HG				
	BEFORE OPER. FEMORAL B. P. MM. HG	AFTER OPERATION OF CLAMPING AORTA			
		TIME (IN HOURS)	CAROTID (B. P. MM. HG)	FEMORAL (B. P. MM. HG)	PULSE RATE
22	120	Uninephrectomy and Abdominal Aorta Clamped			
	116	144	110	86	78
	134	Aorta Clamped at Level of Dome of Diaphragm			
	112	168	144	54	90
	125	192	153	65	90
	117	Remaining Kidney Removed			
	128	198	95	—	96
	106	242	114	64	112
	120	266	123	50	100
		Blood Urea Nitrogen 105 mg. for 100 c.c.			
		290	132	56	98
		Blood Urea Nitrogen 156 mg. for 100 c.c.			
		314	132	60	120
		Blood Urea Nitrogen 215 mg. per 100 c.c.			
23	138	Uninephrectomy and Abdominal Aorta Clamped			
	140	Aorta Clamped 4 cm. Below Dome of Diaphragm			
	130	96	172	80	64
	132	120	177	78	72
		Remaining Kidney Removed			
		134	150	60	70
24	140	Uninephrectomy and Abdominal Aorta Clamped			
	125	Aorta Clamped 5 cm. above Dome of Diaphragm			
	133	120	156	108	80
	146	168	160	107	86
	135	288	151	120	84
		Clamp on Abdominal Aorta Tightened			
		336	154	110	88
		360	168	106	86
		Remaining Kidney Removed			
		384	170	92	104
		408	156	94	100
		Blood Urea Nitrogen 106 mg. per 100 c.c.			
		432	170	90	110
		Blood Urea Nitrogen 168 mg. per 100 c.c.			
		456	166	92	90
		Blood Urea Nitrogen 221 mg. per 100 c.c.			
		480	130	88	62
		Blood Urea Nitrogen 299 mg. per 100 c.c.			
25	132	Uninephrectomy and Abdominal Aorta Clamped			
	124	Aorta Clamped Level with Dome of Diaphragm			
		120	146	98	84

kidneys, definite hypertension was found to occur in the carotid vessels (Dogs No. 20 to 25). Usually the clamp on the thoracic aorta did not reduce the femoral blood pressure much further than had the abdominal one. In two animals (No. 21, 22), after nephrectomy the arterial pressure fell sharply to normal, and, in the remaining two (No. 23, 24), the fall was slow.

Effect of Clamp on Arch of Aorta.—Either one or two clamps were placed on the aortic arch; in the latter case the first clamp was about one-half closed, and, four to seven days later, the second one was applied and almost or completely closed. The dogs died of rupture of the aorta

TABLE III

EFFECT ON CAROTID AND FEMORAL ARTERIAL PRESSURE OF CLAMPING THE ARCH OF THE AORTA

DOG NO.	INTRA-ARTERIAL BLOOD PRESSURE MM. HG				
	BEFORE OPER. FEMORAL B. P. MM. HG	AFTER OPERATION OF CLAMPING AORTA			
		TIME (IN HOURS)	CAROTID (B. P. MM. HG)	FEMORAL (B. P. MM. HG)	PULSE RATE
26	148	Clamp partially closed			
	144	–	–	–	–
	166	72	–	–	–
	150	Clamp closed			
		96	144	104	78
		120	135	102	72
27	150	Clamp one-half closed			
	130	24	156	122	78
	160	48	160	108	78
	152	72	150	78	80
	137	96	166	64	80
	140	120	128	30	78
	150				
28	140	Clamp one-half closed			
	152	–	–	–	–
	144	96	–	–	–
	154	Closed			
		120	156	92	100
		Ruptured aorta			
29	136	First clamp			
	140	Second Clamp, 5 days later			
	144	¼	–	102	90
		24	136	110	80
		72	149	130	84
		168	162	128	80
		Died 12 days after 2nd clamp			
30	109	First clamp			
	108	Second clamp, 6 days later			
	115	¼		100	–
		72	114	55	70
		Died 4 days after 2nd clamp			
31	130	Clamp three-quarters closed			
	107	–	–	–	–
		24	–	–	–
		Closed			
		48	138	58	52
		72	124	40	60
32	138	96	115	99	150
	134				
	130				
33	156	Clamp one-half closed			
	124	24	144	136	90
	130				
	139				
34	158	Cellophane wrapped around arch of aorta			
	160	Clamped 22 days later			
	104	96	133	116	84
	120	120	158	140	76
	146				
	132				
	128				
	120				
	124				

in from three to twelve days. None of the animals developed hypertension. The pressure in the femoral artery was reduced as much as when the abdominal and lower thoracic aorta was clamped. The oxygen content of the blood was reduced to 12.25 volumes per cent in only one animal in which the femoral pressure was reduced to 40 mm. Hg while the carotid pressure remained at 124 mm. Hg.

Oxygen Content of Shunted Blood.—In a few experiments the oxygen content of the blood from the femoral artery was ascertained by Sendroy's[21] (1931) modification of the method of Van Slyke[22] (1918). Twenty-four hours after clamping the arch of the aorta in Dog No. 27, the oxygen content was 20.4 volumes per cent and the femoral arterial pressure was 122 mm. Hg. Seventy-two hours after clamping, the femoral pressure had fallen to 78 mm. Hg, yet the oxygen content was still 19.3 volumes per cent. A further fall to 64 mm. Hg again was not accompanied by a significant fall in oxygen content (19.1 volumes per cent). The femoral arterial pressure had to be greatly reduced before the oxygen content fell. For example, the aorta at the arch was closed in Dog No. 31, and the femoral pressure was reduced to 40 mm. Hg. The oxygen content was 12.25 volumes per cent.

DISCUSSION

Our results demonstrate that the production of hypertension in dogs by constricting the aorta depends on the site of the constriction. If it is below the origin of the renal vessels, hypertension does not occur, but if just above, hypertension is readily produced, as Goldblatt and Kahn[12] (1938) have shown in dogs, and Rytand[16] (1938) in rats.

Constriction at the level of the dome of the diaphragm, or slightly below, caused only slight, transient hypertension, or none at all. If, however, the abdominal aorta just below the origin of the renal arteries had at a previous operation been tightly constricted or occluded, and a second clamp was then applied low in the thorax, hypertension resulted. Severe constriction of this sort often led to renal insufficiency.

When one or two clamps were applied to the descending portion of the arch of the aorta—at the point where coarctation in human beings occurs—no hypertension was found proximal to the clamp. In most such experiments it was necessary to apply one clamp and constrict the aorta partially at the initial operation; otherwise, death occurred within a few hours. Several days later a second clamp was applied about 2 cm. below the first, and almost, or completely, closed. Apparently the first clamp aided in the formation of collateral circulation, so that closure of the aorta was tolerated.

The carcasses of some of the animals were injected with barium sulfate-acacia solution and roentgenograms made. These demonstrated in striking fashion the extensive collateral circulation. This was verified by anatomic dissection. At operation for application of the second clamp

the extensive collateral circulation was readily seen in the intercostal muscles and caused ubiquitous bleeding.

The rise toward normal in femoral pressure which may occur a few hours after clamping the aorta probably has several causes, but at present it is not possible to be sure which is the most important. Opening large collateral channels would appear to aid in returning blood to the portion of the aorta distal to the clamp. Augmentation of the cardiac output might also aid. Barcroft[17] (1931) has shown that, in acute experiments, occlusion of the aorta leads to an increase in cardiac output. It is of interest to note that the pulse rate tended to be somewhat slower than normal after the clamp had been applied.

It has seemed to us that an important cause for the return of blood flow to normal was the decrease in thickness of the vessel wall within the clamp, caused by stretching, and atrophy and necrosis which result from the pressure of the clamp on the arterial wall. The stretching may occur shortly after applying the clamp, and hence may contribute to the immediate increase of flow through the clamp. Atrophy and necrosis require longer to develop, and may contribute to the increase observed in chronic experiments. Dr. Paul Harris and Dr. Irving Graef have examined several aortae which had been clamped, and report marked atrophy of the muscle cells, with intact, though condensed, elastic layers. The same sort of change was found in the renal vessels when a clamp had been applied to them. In many animals it has been observed that the walls of the vessel within the clamp are paper-thin. Indubitably, such a change must lead to an increase in the amount of blood which can pass through the clamp. This may in part be the cause of the successive rises of pressure in the renal artery observed by Schroeder and Cohn[23] (1938) following repeated constrictions.

The pressure in the femoral artery by no means always rises after the first day following clamping. With the passage of time a marked fall may occur (Dog No. 27, for example), with a concomitant fall in carotid arterial pressure. This may be caused by clot formation within the clamped portion of the aorta, a condition which we have repeatedly found at autopsy.

The results of our experiments on the oxygen content of the blood suggest that the shunting of blood is a relatively efficient process, not necessarily accompanied by great loss of oxygen from the blood completing the circuit around the constricted or occluded area of the aorta.

Measurements of the extent of constriction required to reduce pressure significantly showed that from 65 to 80 per cent of the original cross section of the artery must be obliterated. These results confirm those of Mann, Herrick, Essex, and Baldes[20] (1938).

The ability of dogs to develop collateral circulation, and hence to compensate for the occlusion of arteries supplying large vascular areas, is extraordinary. Blalock and Levy[24] (1939) found that the celiac axis

and the superior and inferior mesenteric arteries can be gradually occluded without causing death or permanent impairment of health. Sustained hypertension did not occur. If, in such animals, *one* renal artery is clamped, the result is prolonged and marked hypertension of a degree seldom observed when the mesenteric vessels and celiac axis are not constricted (Blalock, Levy, and Cressman,[25] 1939). Goldblatt, Kahn, and Hanzal[15] (1939) found that it was often necessary to apply a clamp to the renal artery to sustain hypertension after it had developed as a result of constriction of the aorta close to the openings of the main renal vessels. Our experiments show that when the constriction is well away from the renal vessels, hypertension does not result. If it is sufficiently close and complete enough, hypertension of renal origin occurs, for removal of the kidneys reduces or abolishes it. It seems reasonable to believe that constriction of the vessels in the immediate neighborhood of the renal vessels, as all these experiments show, aids in preventing the development of an adequate collateral circulation, and hence intensifies the hypertension produced by clamping the renal vessels, or produces hypertension if it was not already present.

Apparently, dogs are able to develop sufficient collateral circulation when the aorta is constricted or occluded in the upper thorax to prevent the stimulus to the kidneys which results in hypertension. It does not appear that the complete clinical picture of coarctation similar to that in human beings has been reproduced in animals. Partial occlusion of the aorta close to the site of origin of the renal vessels does not duplicate the anatomic lesion of human coarctation, although the hemodynamic changes which result appear to resemble those observed in coarctation in man.

Human beings, also, are apparently able to develop collateral circulation to the kidneys. This is well illustrated by three remarkable patients described by Fry[26] (1939). In one, the aorta was chronically occluded by an old and well-organized thrombus just below the diaphragm. The right renal artery was patent, and the left partially patent. The celiac axis was occluded, and both common iliac arteries were thrombosed throughout their length. The arterial pressure was normal over a period of three years, and only rose shortly before death, when it was found to be 190/100 mm. Hg in the right arm and 144/100 mm. in the left. In a second patient the occlusion was immediately below the origin of the renal arteries. The arterial pressure was 198/96 mm. Hg. In a third case, an organized thrombus obstructed the aorta completely at the level of origin of the left renal artery. The right renal artery was patent, and the left partially occluded. The upper pole of the left kidney was scarred by a large infarct. The arterial pressure was normal. Evidently, extensive obstruction of the aorta can occur in human beings with moderate or no hypertension, even though the obstruction is in the region of the site of origin of the renal vessels.

SUMMARY

The aortae of dogs may be constricted or occluded at the arch without the development of arterial hypertension proximal to the occlusion. Hypotension of moderate to marked degree occurs distal to the occlusion, and is usually more marked a few hours after clamping than later. The return toward normal of the pressure distal to the clamp was attributed, among other causes, chiefly to the development of collateral circulation and acute and chronic thinning of the vessel walls within the clamp. After several days the pressure in the femoral artery may fall progressively, without simultaneous reduction of carotid pressure. The oxygen content of the blood does not appear to be reduced significantly until a great reduction of femoral pressure has occurred.

The failure to produce, in dogs, hypertension proximal to a clamp constricting the aorta at or near the site where aortic coaretation occurs in human beings is attributed to the ready development in dogs of an extensive collateral circulation.

Hypertension of renal origin occurs when the aorta is closed a few centimeters below the origin of the renal vessels, and, in addition, constricted or closed in the thorax at a level corresponding to the dome of the diaphragm. Removal of the kidneys reduces or abolishes this hypertension. The hemodynamic changes are sufficiently similar to suggest the possibility that the hypertension of human coaretation is of renal origin, and that the manner in which collateral circulation develops differentiates the response to constriction of the aorta in dogs and men.

Mr. Roland Parker gave able technical assistance in the conduct of these experiments.

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DESCRIPTION OF A NEW PLETHYSMOGRAPH

EUGENE B. FERRIS, JR., M.D., AND DAVID I. ABRAMSON, M.D.
CINCINNATI, OHIO

OF THE various procedures at present employed in the study of peripheral blood flow in health and disease, it appears fairly well established that the plethysmographic method is superior in many respects. This procedure has been utilized in numerous studies since 1935, when Freeman[1] described an accurate and practical hand plethysmograph. More recent investigations[2, 3, 4, 5] have revealed, however, that the blood vessels in different portions of the extremities react differently to various stimuli, which makes it desirable to investigate more than one vascular bed. For this purpose we have constructed a plethysmograph which can be utilized to study the blood flow and volume changes in the hand, in the forearm, or in the leg.

DESCRIPTION OF APPARATUS

The plethysmograph consists of an inner brass cylinder, 5½ inches long and 6 inches in diameter, which is open at both ends and is enclosed by another cylinder of the same length and material, but with a diameter of 7 inches (Fig. 1). In this fashion, an insulated space, which is sealed at both ends, is formed (Fig. 1*B:6*). There are three openings on the top, which are continuous with the inner chamber (Fig. 1*C:1, 2, 3*). On one side of the apparatus is a double-walled box of brass, the inner space of which also opens into the large chamber (Fig. 1*C*). In this side box are an electric immersion heater, running the length of the space (Fig. 1*C:8*), and a propeller with three short blades (Fig. 1*C:7*). This propeller is attached to a shaft which penetrates the wall of the side compartment through a packing box, to prevent leaks, and it is joined to the shaft of a motor by a flexible coupling (Fig. 1*A:5*). The motor contains a reducing gear, so that the final speed is 100 revolutions per minute. The outer wall of the side compartment (Fig. 1*A:2*) is so constructed that it, together with the packing box and propeller, can be removed en masse by loosening the screws which hold it in position. The joint is made watertight with the aid of a rubber gasket. In this fashion, repair of the heater or propeller can be effected, if necessary, with little inconvenience. At the lower angle of the side compartment is a tube which penetrates the insulated space; it is used to drain the water from the plethysmograph (Fig. 1*A:4*). In the upper portion of the side compartment is a brass tube which runs the full length of the space, parallel to, and above, the heater, and opens to the outside at both ends (Fig. 1*A:3*). The thermostat is inserted into this brass tube. Two slotted rods are soldered to the sides of the main inner cylinder in its upper portion (Fig. 1*C:4*). Through these are inserted two solid rods, each attached along its full length to one edge of a hammock of brass screening (Fig. 1*B:1*). A number of hammocks are necessary, in order that one can be used which conforms to the size and shape of the portion of the extremity being studied.

From the Department of Internal Medicine, College of Medicine, University of Cincinnati, the Cincinnati General Hospital, and the May Institute for Medical Research of the Jewish Hospital, Cincinnati, Ohio.

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To each end of the outer wall are soldered two extensions (Fig. 1*B:3*) containing a threaded hole for the insertion of a thumb screw; the latter is used to maintain one of the leaves of a slotted aluminum iris diaphragm in position (Fig. 2*A:1, 4*). Each of these leaves is cut out to conform to half of the circumference of the extremity at the point of entrance to, or exit from, the plethysmograph. A number of sets of different sizes are necessary for the various portions of the extremities.

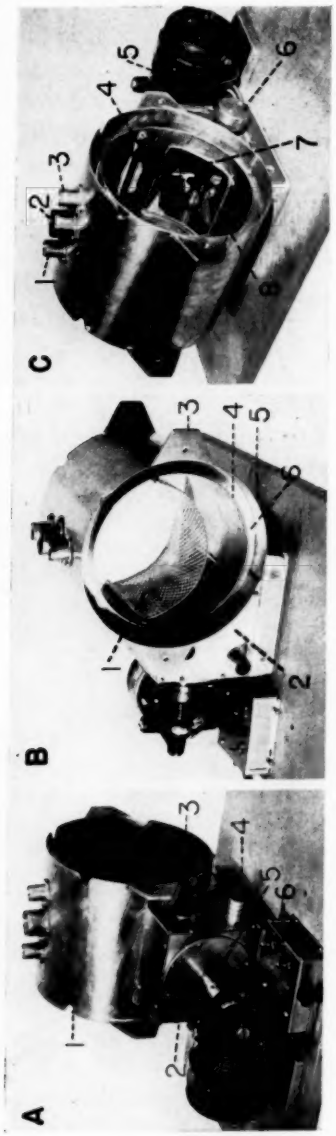

Fig. 1.—*A*, Side view of the plethysmograph. (1) Slot in cylinder facilitating removal of iron ring; (2) outer wall of side compartment, which can be removed by loosening screws; (3) space for insertion of thermostat; (4) drain tubing; (5) flexible coupling connecting shaft of propeller to motor; (6) switch box.

B, Anteroposterior view. (1) Hammock of brass screening; (2) side compartment; (3) extension for support of iris diaphragm; (4) edge of inner cylinder over which iron ring fits; (5) edge of outer cylinder; (6) brass wall closing the two ends of insulated space.

C, Oblique view. (1) Opening for calibrating burette (this is unnecessary if drain tube is utilized for calibration); (2) opening for wide glass tube connected to Brodie's bellows; (3) opening for thermometer; (4) slotted rod for insertion of solid rod attached to hammock; (5) motor; (6) outer view of heater; (7) propeller blade in side compartment; (8) inner view of heater.

Two cast iron rings, each slightly larger than the diameter of the inner cylinder (Fig. 1*B:4*), are utilized to hold the rubber membranes in place over the openings. The difference between the diameter of the rings and that of the edge of the cylinder is sufficient to allow a rubber membrane, 1/64″ in thickness, to be utilized as the diaphragm through which the extremity passes. Two slots are made at each end

of the outer cylinder in order to allow the insertion of a rod, bent at one end, for the purpose of removing the iron ring from the inner cylinder at the completion of the experiment (Fig. 1*A:1*).

In order to utilize the plethysmograph for the study of blood flow in the hand (Fig. 2*A*), one end of the machine is temporarily closed by stretching a rubber membrane over the opening and preventing it from bulging by the use of a wooden

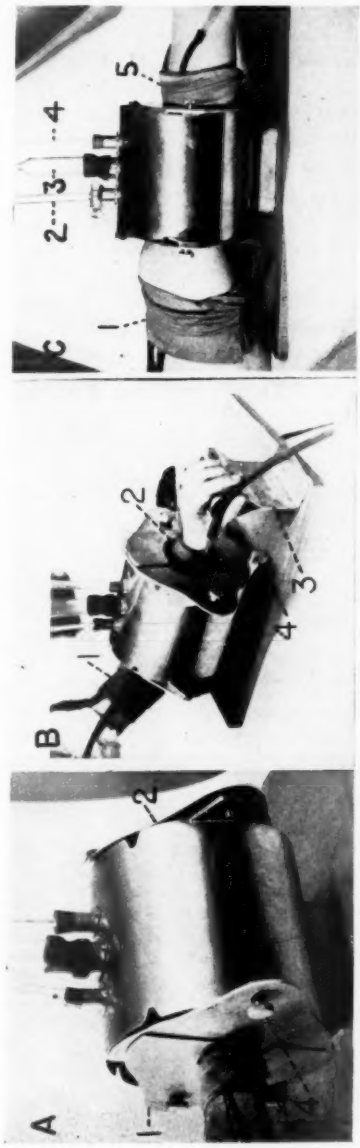

Fig. 2.—*A*, Apparatus used as a hand plethysmograph. (1) Leaf of iris diaphragm; (2) one end of apparatus closed off by means of rubber diaphragm, wooden disc, felt pad, and iris diaphragm; (3) blood pressure cuff at wrist, utilized in the production of a venous occlusion pressure; (4) thumb screws used to maintain iris diaphragm in position.

B, Apparatus used as a forearm plethysmograph. (1) Blood pressure cuff utilized in the production of venous occlusion pressure; (2) blood pressure cuff at wrist, maintained at a pressure of 300 mm. Hg during observations; (3) support for hand; (4) portion of rubber diaphragm beyond ring.

C, Apparatus used as a leg plethysmograph. (1) blood pressure cuff above knee, utilized in the production of a venous occlusion pressure; (2) calibrating burette; (3) wide glass tube; (4) thermometer; (5) blood pressure cuff at ankle, maintained at a pressure of 300 mm. Hg during observations.

disc slightly smaller than the ring. A felt pad is then placed against the wooden disc, and held in position by means of the iris diaphragm (Fig. 2*A:2*). The hand is inserted into the machine as far as the wrist, and rests on the brass screening. All other steps in the preparation for blood flow determinations are similar to those previously described by one of us.[6]

In using the apparatus to study blood flow in the forearm (Fig. 2*B*), the extremity is placed in the machine so that the hand extends beyond the opening and rests on an aluminum support (Fig. 2*B:3*). In this respect the plethysmograph differs from those previously described, since in these the hand is always immersed in water at the same temperature as that in the chamber containing the forearm. This step has not been found necessary, because, during maintenance of a pressure of 300 mm. Hg at the wrist (Fig. 2*B:3*), alterations in the caliber of blood vessels in the hand can no longer influence blood flow in the forearm. When it is desired to use the apparatus for the study of blood flow in the leg (Fig. 2*C*), the wire hammock is first removed, and the leg is inserted into the machine so that the foot extends beyond it, where it is supported on a pillow. An appropriately shaped hammock is then reinserted to allow the portion of the leg in the machine to rest on it, and the knee is also maintained in position by the use of a pillow or sand bag.

The three openings on the upper surface of the plethysmograph are used for the insertion of a calibrating burette, a glass tube about 1 inch in diameter, and a thermometer (Fig. 2*C: 2, 3, 4*); the glass tube is connected to a Brodie's bellows by means of rubber tubing. If desired, the opening for the calibrating burette can be closed or eliminated, and the apparatus calibrated by utilizing the drain outlet at the lower angle of the side compartment (Fig. 1*A:4*). This is done by connecting the outlet to a glass Y tube, one limb of which is attached to a 10 c.c. syringe.

Since both ends of the apparatus are of the same diameter, the plethysmograph can be reversed, in order to keep the motor and side compartments away from the subject, regardless of whether the extremities on the right or left side are studied. By means of the immersion heater, paddle wheel, and thermostat, the temperature of the water can be readily maintained at any desired level.

SUMMARY

A new plethysmograph,* which can be utilized in the study of blood flow in the hand, the forearm, or the leg, is described.

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*The apparatus was constructed by the Kruger and Hudepohl Co., Cincinnati, Ohio.

Department of Clinical Reports

SHORT PAROXYSMS OF IMPURE AURICULAR FLUTTER PROBABLY INDUCED BY NORMAL SINUS BEATS

HANS HECHT, M.D., AND FRANKLIN D. JOHNSTON, M.D.
ANN ARBOR, MICH.

THE occurrence of auricular flutter in patients with complete A-V heart block is not common, but almost thirty such cases, including the first case of flutter ever described, that of Ritchie,[1] have been found in the literature and are discussed in papers by Routier, Mamon, and Le Mant,[2] and by Jourdonais and Mosenthal.[3] Ten more examples of the condition must be added if similar cases reported by Canessa,[4] DiGregorio and Crawford,[5] Israel,[6] Ludwig and Bener,[7] Singer and Winterberg,[8] and the cases of impure flutter and A-V block reported by Solomjany and Boukspan[9] and Lian and Welti[10] are included. We believe that the patient who is the subject of this report is of unusual interest because her electrocardiograms on different occasions showed auricular fibrillation and auricular flutter with complete A-V dissociation, and, on one occasion, very short paroxysms of auricular flutter, apparently initiated by normal sinus impulses, could be observed.

REPORT OF CASE

The patient, a housewife of 52 years, entered the hospital Sept. 16, 1938, complaining chiefly of attacks of dizziness and fainting spells which had been associated with bradycardia. She felt well until 1934, when, with the beginning of the menopause, she noticed dizziness for the first time. Her first fainting spell, however, occurred early in 1938, and thereafter the attacks had become frequent and severe. She had been unable to do her housework during the preceding summer.

The past history was of no importance, aside from the fact that she had had a thyroidectomy at the age of 22 years because of "toxic goiter." At this time she noticed weight loss, nervousness, and slight exophthalmos.

Physical examination revealed a well-developed, well-nourished woman who was not acutely ill; the examination was negative except for the features noted below.

The thyroid gland was palpable, and there was a nodule the size of a walnut slightly to the right of the isthmus. The heart was slightly enlarged, with the left border of cardiac dullness 10 cm. to the left of the midsternal line in the fifth intercostal space. On admission, the ventricular rate was approximately 40 per minute, and no irregularities were present. A soft systolic murmur, transmitted to the axilla, was heard at the apex, but no diastolic murmurs were audible. The blood pressure measured 170/70 in both arms.

The urine was normal, and the blood Kahn test was negative. The orthodiagram showed a 38 per cent increase in the cardiac area, and an increase in the

From the Department of Internal Medicine, University of Michigan Medical School. This study was assisted by a grant to Dr. F. N. Wilson from the Horace H. Rackham School of Graduate Studies.

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transverse diameter of 18 per cent over the predicted normal (Hodges-Eyster formula). The basal metabolic rate was minus 1 per cent.

During the first few days of her hospital stay she had several minor fainting spells, and electrocardiograms taken during this period (Fig. 1) showed 2:1 A-V heart block and right bundle branch block. She received 0.025 Gm. of ephedrine sulphate and 0.05 Gm. of sodium amytal four times daily, with occasional injections of adrenalin, during this period, but this treatment was not effective, and, on Sept. 20, she became stuporous with a heart rate between 20 and 30 per minute. At this time a number of electrocardiograms were taken, and it will be seen (Fig. 2*A* and *B*) that complete A-V dissociation was present, and that within a period of a few minutes transitions from auricular fibrillation (Fig. 2*A*) to flutter (Fig. 2*B*) and then to slow sinus rhythm, with short paroxysms of what

Fig. 1.—Standard electrocardiograms, taken soon after patient's admission to the hospital, showing 2:1 A-V heart block and right bundle branch block.

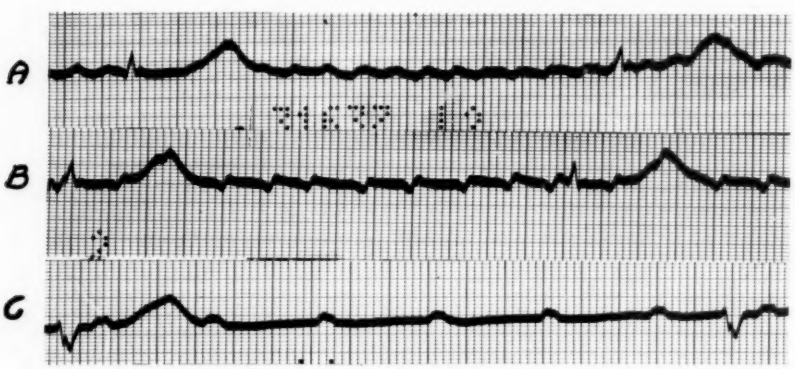

Fig. 2.—*A*, *B*, and *C* are strips of standard Lead II, and show complete A-V dissociation. *A* shows auricular fibrillation, and *B*, auricular flutter. In *C*, normal sinus activity and a slow idioventricular rhythm were present most of the time. Occasional responses to the auricle, not shown in the figure, occurred at this time.

appears to be auricular flutter, occurred (Fig. 3). During the first part of the continuous strip in Fig. 3, a paroxysm consisting of fifteen circus waves is seen, and much shorter runs of the peculiar rhythm are shown in Fig. 3*B* to *E*. In every instance the onset of the circus rhythm was linked by the same interval to a P wave of normal appearance. This unusual auricular rhythm was present for a few minutes only, and a curve taken shortly thereafter (Fig. 2*C*) showed a slow idioventricular rhythm with occasional responses to the auricle. Later, 2:1 and 3:2 heart block appeared.

The patient had many syncopal attacks during the next few days, and, in spite of frequent injections of adrenalin, the ventricular rate varied from 17 to 45 per minute. On Sept. 24, she was given desiccated thyroid gland, in addition to other drugs. Within a few days the ventricular rate gradually increased and her attacks disappeared, and an electrocardiogram taken on October 4 (Fig. 4) showed right bundle branch block with normal sinus rhythm. On October 8, all drug therapy was discontinued, but nevertheless the patient felt well and had no further fainting spells for a period of eight days, at the end of which time she was discharged from the hospital. After her return home she got along satisfactorily for almost three weeks, when, following psychic trauma, the spells of faintness recurred, and she was readmitted to the hospital Nov. 9. While at home she had received no thyroid medication, and was given none until Nov. 26.

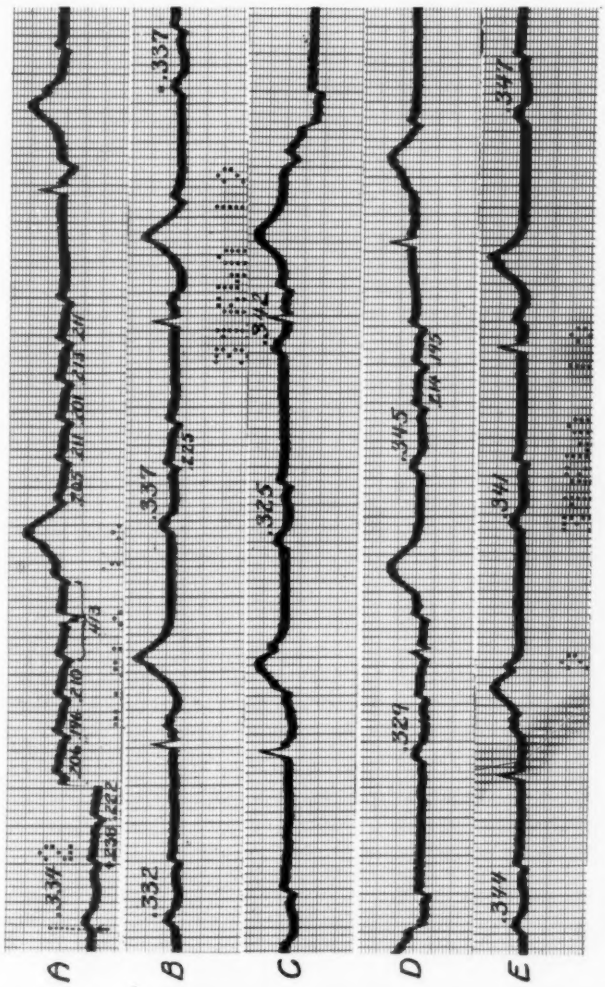

Fig. 3.—Continuous strips of standard Lead II are shown in *A* through *E*. The figures marked in ink above the curves represent the time (in seconds) from the beginning of a P wave to the downward peak of the circus wave that follows it. The figures below the tracings give the time between successive circus movements.

During her second hospital stay her heart rate averaged from 40 to 45 per minute before thyroid was given, and 55 per minute thereafter, and no episodes of complete A-V block or abnormal auricular rhythm occurred. The electrocardiograms showed right bundle branch block and 2:1 A-V block, and were similar in all respects to the curve shown in Fig. 1.

COMMENT

Some of the clinical findings are of particular interest. Without question this patient had organic heart disease, probably of hypertensive-arteriosclerotic origin, but the short periods of complete A-V dissociation and auricular arrhythmia which were observed during her first hospital stay were not precipitated by infection or other obvious cause. Ephedrine and adrenalin were not as effective as usual in establishing idioventricular rhythm and preventing marked bradycardia. Only after she began to receive thyroid extract did her condition improve. It is difficult to be sure that the improvement during thyroid treatment was due to the drug, however, for she was asymptomatic for at least four weeks after the medication was stopped. Willius[11] has pointed out several times that patients with A-V heart block and Adams-Stokes attacks may be greatly benefited by thyroid therapy even when thyroid gland function is apparently normal, and it is possible that thyroid was effective in this case.

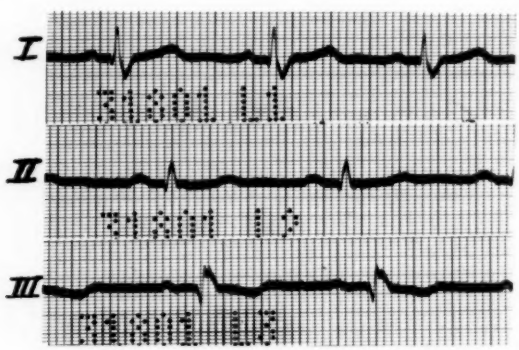

Fig. 4.—Standard electrocardiograms, taken ten days after thyroid medication was started. Normal sinus rhythm and right bundle branch block are present.

Short paroxysms of auricular fibrillation or flutter, in man, have been observed by several workers. Wolferth[12] described the electrocardiograms of two patients showing the latter condition and was able to study the effect of vagus stimulation and different drugs on the duration of the paroxysms. In his patients the attacks of circus rhythm were precipitated by auricular premature beats, whereas in two cases reported by Semerau[13] the attacks were thought to be initiated by normal sinus impulses. It is generally believed that, in man, both fibrillation and flutter are usually precipitated by auricular extrasystoles. Such beats cannot induce circus rhythm unless the auricular muscle is in the so-called "fibrillary state," and, although such a condition is most likely to exist at the time of a premature beat, there is no reason to believe that an impulse arising in the sinus node is incapable of precipitating circus movement.

Several features of the tracings shown in Fig. 3 indicate that short paroxysms of flutter induced by normal auricular beats occurred in

our patient. That the oscillations in question were produced by circus movement is suggested by the saw-tooth form of the waves and by their similarity to those seen in Fig. 2*B*. In both figures there are slight variations in the outline of the oscillations and in the auricular rate, so that impure flutter, with changes in the path of the circus movement, was probably present. All of the short paroxysms that were recorded are shown in Fig. 3, and in all instances they follow P deflections of normal outline. Measurements of the time from the beginning of these P waves to the downward peak of the succeeding circus oscillation were made wherever these intervals could be accurately determined. These intervals are indicated above the tracings in Fig. 3, and it will be seen that the difference between the longest (.347 sec.) and the shortest (.325 sec.) of these is only slightly over 0.02 sec. There can be little doubt, in our opinion, that the short paroxysms of flutter were induced by auricular beats arising in, or near, the sinus node.

Experimental evidence supporting the foregoing is found in observations made by Lewis, Feil, and Stroud.[14] They observed that when rapid, rhythmic, induction shocks, applied to a dog's auricle, were increased in rate until evidences of faulty conduction appeared, and then suddenly stopped, aftereffects, consisting of auricular fibrillation or flutter, regularly occurred. The circus rhythm thus induced might be of extremely short duration or it might last for one-half hour or longer. In one animal (dog KD), after rhythmic stimulation, a single afterbeat, believed to represent a single circus movement, occurred. Normal rhythm then returned, but for several cycles each normal beat was followed by an ectopic response, and these premature beats were separated from the normal beats by the same interval as the cycle preceding the single afterbeat. This led the authors to believe that these single premature beats were also caused by circus movement, precipitated, in this instance, by a natural heartbeat.

It is possible that in our patient the auricular fibrillation and flutter which were present shortly before the curves of Fig. 3 were taken had a depressant effect on muscular conduction analogous to the effect of rapidly recurrent shocks on the dog's auricle, and that the paroxysms described are similar to the aftereffects noted in dogs after such stimulation. Few electrocardiograms have been taken immediately after attacks of circus rhythm in man, so that it is not known whether or not these aftereffects are of frequent occurrence. Other influences tending to depress conduction in this patient's heart were probably present during the time when both auricular fibrillation or flutter and complete A-V dissociation were observed, and it is possible that the short episodes of circus rhythm occurred while the state of depressed conduction was passing off.

The paroxysms of circus movement that have been described were of such short duration that there was no opportunity to try the effects of carotid sinus stimulation or of any other procedures. It is possible

that reflex vagal stimulation might have caused longer paroxysms in our patient, as it did in the first case described by Wolferth. Carotid sinus stimulation in this patient on other occasions, however, was without obvious effect upon A-V conduction or upon the auricular rate. Measurements of the cycle lengths during circus rhythm are shown beneath the tracings in Fig. 3. The only paroxysm long enough to enable one to say much about the mode of termination is the first one, consisting of fifteen circus movements (Fig. 3*A*). In this instance the paroxysm stopped abruptly, without appreciable change in cycle length. In the paroxysm consisting of three cycles of circus movement, seen in Fig. 3*D*, there is slight reduction of cycle length with the termination. We do not believe there are enough data here to justify speculation concerning the factors involved in the termination of the paroxysms.

SUMMARY

Electrocardiograms of a patient with transient auricular fibrillation and flutter and complete A-V heart block are presented. Further tracings, taken immediately after the resumption of normal sinus activity, show short paroxysms of what is believed to be impure flutter induced by normal sinus beats. Some experimental evidence tending to support this view is mentioned.

The authors wish to thank Dr. F. N. Wilson for his assistance in the preparation of this paper.

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Correspondence

To the Editor:

In a recent paper in the Journal (Activities Associated with the Onset of Acute Coronary Artery Occlusion **18**: 434, October, 1939), Master, Dack, and Jaffe, for the second time, attempt to refute by two arguments my hypothesis that capillaries in atherosclerotic plaques of coronary arteries may rupture and produce intimal hemorrhage and coronary thrombosis because of the transitory rise in blood pressure which accompanies exertion or excitement.

They state that (1) "*Capillary, and even intimal, hemorrhages occur in shock in which the blood pressure drops to very low levels.*" Admitting for the sake of argument that intimal hemorrhages are produced by shock, and there is no proof that they are, I do not see how the associated arterial hypotension can be blamed. The leakage of plasma (and blood) into the tissues in shock is attributed by physiologists to increased permeability of the capillaries, not to low arterial blood pressure. Further, it has been suggested by some physiologists that, in the later stages of shock, the capillary pressure rises and the transudation of fluid from the vessels is increased (Best and Taylor, page 417).

Master and his co-workers state further that (2) "*Winternitz, et al., injected dye into sclerotic coronary arteries at pressures varying from 500 to 1,000 mm. Hg without producing rupture of the intimal capillaries. Surely the pressure in the coronary arteries and capillaries during life is very much lower than this, so that hypertension cannot be a factor in intimal hemorrhage.*" I am afraid that one cannot compare the effect of pressures present in the coronary arteries during life with those used in injecting the coronary circulation after death. For example, the ostia of intimal capillaries after death may be partially obstructed by post-mortem clot, so that the injection fluids do not enter freely. Winternitz allowed his specimens to stand in a preservative solution (thymol) for twenty-four hours before injecting them. One must therefore consider the effect of a preservative on the fragility of intimal capillaries and on the rigidity of their supporting stroma.

I cannot agree with Master and his co-workers when they say that intimal hemorrhage is "*probably a fortuitous event.*" I prefer to believe that intimal capillaries rupture as the result of certain definite causes, each of which we should search for industriously. Until these causes are known and proved beyond doubt, it would seem wiser to assume that an intimal capillary ruptures partly as the result of pressure within its lumen, and to continue advising all patients with coronary disease to avoid excessive exertion or emotion or any other activity which may raise unduly their intracapillary pressure.

J. C. Paterson, M.D.,
Department of Pathology,
Civic Hospital,
Ottawa, Canada.

To the Editor:

The problem of the initiation of coronary artery occlusion is of great importance, but difficult to study experimentally. We attacked the problem by making a detailed investigation of patients' activities for several days and weeks prior to, and attending, the onset of attacks. First, the results of our study of 800 attacks were published (J. A. M. A. **109**: 546, 1937), and recently the series was extended to 1,440 attacks (Am. Heart J. **18**: 434, 1939). It was found that the majority of attacks occurred during sleep, rest, or mild activity, and only 2 per cent were associated with unusual exertion. On the basis of these facts, it was concluded that intimal hemorrhage, usually the first step in the process of occlusion, was independent of external factors. It is a late stage in arteriosclerosis.

In contrast to this conclusion, based on clinical observations, Paterson has postulated that the intimal hemorrhage results from a transitory rise in blood pressure accompanying exertion or excitement. We have pointed out that this "hypothesis," usually referred to by him as a fact, was entirely without experimental or clinical confirmation, and, indeed, was controverted by our findings. It was our contention that his assumption could not be considered valid as long as there was no proof whatever that a rise in aortic pressure increased the pressure in the intimal capillaries to an extent sufficient to cause them to rupture. In any case, the absence of a history of exertion in relation to the attacks in our large series excluded exertion as a factor in the initiation of intimal hemorrhage.

Incidentally, we mentioned two additional facts which seemed inconsistent with Paterson's hypothesis; namely, the occurrence of intimal hemorrhage in shock, and its failure to occur following the injection of dye into sclerotic coronary arteries at high pressures, as performed by Winternitz, et al. Paterson cites these arguments as if they were the only ones against his theory which we presented, whereas actually they are merely isolated experimental facts, not related to our main argument as previously stated. His objections, therefore, are not fundamental. Furthermore, we do not believe they are valid. In regard to shock, we did not state that a fall in blood pressure produced intimal hemorrhage, but merely intimated that this was as logical as his theory concerning an increase in blood pressure. Although we do not accept their conclusions, we may cite Luten (Contributory Factors in Coronary Occlusion; Am. Heart J. **7**: 36, 1931) and Pepper (Hypotension; Northwest Med. **34**: 325, 1935), who believe that, in general, a fall in blood pressure favors the formation of coronary occlusion. More specifically, Sprague and White (Nitroglycerin Collapse; Med. Clin. N. A. **16**: 895, 1933) and Prodger and Ayman (Harmful Effects of Nitroglycerin; Am. J. Med. Sc. **184**: 480, 1932) suspect that the fall in blood pressure produced by nitroglycerin may initiate coronary occlusion. In the absence

of any proof of a relationship between systemic blood pressure and intimal hemorrhage, we consider the association of coronary occlusion with a fall or rise in blood pressure as purely coincidental.

Paterson's comments in regard to Winternitz's findings are purely theoretical and inconclusive.

Although Paterson admits that the causes of intimal hemorrhage are not known, and considers his view an "hypothesis," he would accept it as true, and advise all patients with coronary disease to avoid any activity which might raise their intracapillary pressure. This is unwarranted by the facts. Certainly, he must realize that there are millions of people with varying degrees of coronary disease who work regularly, whose blood pressure is raised repeatedly by their everyday activities, yet who do not suffer coronary occlusion. If exertion and emotion were factors in inducing intimal hemorrhage and coronary occlusion, the latter should be exceedingly common. It may be emphasized again that in our series the onset of the attack was associated with severe exertion in only 2 per cent of the cases; if a relation with exertion existed the percentage would be much higher. Furthermore, it is noteworthy that 100 patients in our series, to date, had been bedridden for many weeks or months prior to their attack; surely in these cases the blood pressure did not rise, but probably fell. Another observation is pertinent: in the cases in which death occurred, the incidence of intimal hemorrhages was the same in patients who had never had hypertension as in those who had had hypertension.

We should like to draw attention to a recent paper by Paterson (Capillary Rupture With Intimal Hemorrhage as a Cause of Pulmonary Thrombosis; Am. Heart J. **18**: 451, 1939), in which he explains intimal hemorrhage in the pulmonary arteries on the basis of capillary fragility and minimizes the role of increase in capillary pressure. We believe his reasoning in this instance can be applied with equal force to intimal hemorrhage in the coronary artery.

In our opinion, which is shared by many well-known pathologists, intimal hemorrhage is part and parcel of the atherosclerotic process.

Arthur M. Master, M.D.,
125 East 72nd Street,
New York, N. Y.

Department of Reviews and Abstracts

Selected Abstracts

Viger, T., and Habán, G.: Changes in the Heart and Electrocardiogram in Experimental Hyperthyroidism. Arch. f. Kreislaufforsch. **5**: 49, 1939.

Studies were made on rabbits; nine of these receiving .0025 Gm. thyroxin daily for twenty-four to thirty days and four, .00025 Gm. thyroxin subcutaneously daily for from eighty to 167 days. In all instances a sinus tachycardia developed; T waves became larger at first, then decreased, and then flattened and inverted; a Q wave appeared. The electrocardiographic changes paralleled histological alterations of the heart.

KATZ.

Page, Irvine H.: The Production of Persistent Arterial Hypertension by Cellophane Perinephritis. J. A. M. A. **113**: 2046, 1939.

Severe persistent arterial hypertension has been produced in animals by means of perinephritis induced by cellophane and silk. As a result of the perinephritis a thick, fibrocollagenous, constricting hull is formed around the parenchyma but avoiding the pedicle. Renal ischemia is thus produced by a method different in principle from clamping the renal arteries.

Removal of the offending kidney or the hull around the kidney abolishes the hypertension.

Denervation of the renal pedicle does not prevent the development of hypertension when perinephritis is induced.

Bilateral adrenalectomy in untreated animals abolishes the hypertension. If treated with adequate amounts of sodium chloride and adrenal cortex extract, slight hypertension persists.

The amount of the substance in the blood which combines with renin to form a pressor substance ("renin-activator") is increased.

Perinephritis may be an additional cause of arterial hypertension in man.

AUTHOR.

Page, Irvine H.: On the Nature of the Pressor Action of Renin. J. Exper. Med. **70**: 521, 1939.

Evidence is summarized for the view that experimental hypertension of renal origin is due to liberation of an effector substance from the kidney which appears to be renin. Purified renin has little or no vasoconstrictor action when injected into Ringer's solution perfusing isolated organs, but the pressor action is restored by the addition of a protein-like substance contained in the blood called renin-activator.

The pressor action of purified renin and renin-activator was studied in cats and dogs. Repeated injections of renin resulted in progressively diminishing pressor responses, tachyphylaxis. In general, the greater the amounts of renin injected and the shorter the interval between injections, the more rapidly was tachyphylaxis elicited. The initial blood pressure was not a factor nor was moderate pento-barbital anesthesia.

Strychnine, cocaine, caffeine, infusion of sodium bicarbonate or hydrochloric acid, pithing and intracisternal injection of renin had little effect on the pressor action of renin; nor did the removal of the liver, spleen, and kidneys prevent its pressor effects. Evisceration and large doses of ergotamine reduced the pressor response to renin, while section of the brain may be followed by depressor responses to renin. There was no parallelism between the pressor responses to carotid sinus stimulation, adrenine, and tyramine on the one hand and renin on the other.

Further evidence was presented of the development of tachyphylaxis and the loss of renin-activator by perfusion of blood and small doses of renin in the isolated rabbit's ear, and by continuous infusion of renin in the intact animal.

Renin tachyphylaxis was shown to be due to loss of renin-activator and development of an "antisubstance" (antipressor state or loss of some substance necessary for the chemical reactions which culminate in the pressor action of renin) in the blood. Renin-activator seems an essential constituent of the chemical system responsible for the physiological effects of renin.

The vasoconstrictor effect of the system, renin-renin-activator was exerted primarily by direct action on the blood vessels and except under certain circumstances, was little influenced in experiments of short duration by the removal of the nervous system, endocrine glands, or viscera.

ROTH.

Kabat, Herman: The Cardio-Accelerator Fibers in the Vagus Nerve of the Dog. Am. J. Physiol. **128**: 246, 1940.

Electrical stimulation of the cervical vago-sympathetic trunk and of the vagus rootlets intracranially demonstrates the existence of efferent cardio-accelerator fibers.

The vagal cardio-accelerator fibers are present predominantly if not entirely in the right vagus nerve.

The vagal cardio-accelerator mechanism cannot be excited reflexly by stimulation of the carotid sinus or of the sensory fibers of the vagus nerve or the superior laryngeal nerve.

Acute anemia of the brain excites the vagal cardio-accelerator mechanism.

Acute cephalic anemia increases the rate of the completely denervated heart by a humoral mechanism.

The characteristics of the accelerator response to stimulation of the vagal accelerators indicate that sympathin is probably the chemical mediator at the nerve endings in the heart.

The role of the accelerator fibers of the vagus nerve in the normal regulation of the heart rate is discussed.

AUTHOR.

Herrick, J. F., Grindlay, John H., Baldes, Edward J., and Mann, Frank: Effect on the Blood Flow in the Superior Mesenteric, Renal and Common Iliac Arteries. Am. J. Physiol. **128**: 338, 1940.

The blood flow in the common iliac artery is increased markedly during exercise. The blood flow in the superior mesenteric and renal arteries is not decreased during exercise. With few exceptions, there was either no significant change or a definite increase in the blood flow in the renal artery and the superior mesenteric artery while the dog was running on the treadmill (either horizontal or elevated about 15 degrees) at the rate of three miles per hour for a period ranging from ten to twenty minutes. In a separate study, exercise brought about no decrease in the flow in the splenic artery or in the splenic vein. Our observations allow vasoconstriction in these particular vessels because the increased peripheral resistance may

be counterbalanced by the increased blood pressure so as to effect no significant change in volume flow or an actual increase.

The indirect evidence which led investigators to conclude that exercise brings about a decrease of the blood flow to the kidney and the spleen as well as of that in the superior mesenteric artery is discussed.

AUTHORS.

King, Arthur B.: Nerve Endings in the Cardiac Muscle of the Rat. Bull. Johns Hopkins Hosp. **65**: 489, 1939.

By making frozen sections of tissue perfused during life with methylene blue, it is possible to oxidize the dye adequately and demonstrate nerve cells, nerve fibers, and nerve endings.

Several types of nerve endings were found in the myocardium of the rat; some were interpreted as motor, others as sensory. Complicated terminations encircling muscle fibers were considered to be stretch receptors. These have not been demonstrated before in cardiac muscle.

The mechanism of cardiac pain is discussed. It is suggested that abnormal stimulation of the complicated sensory endings might influence the pain neurones in the posterior gray columns of the cord and produce abnormal sensations interpreted as pain in the chest and arms.

AUTHOR.

Eckey, P.: Studies of the Autonomic Nerve Innervation of the Ventricles in Man. Arch. f. Kreislaufforsch. **5**: 1, 1939.

In a patient with a ventricular parasystole it was found that "Doryl" lengthened the cycle length of the ectopic pacemaker. This also occurred in the period following exercise. Adrenalin had the opposite action. Somewhat similar results were seen in a second case. On the basis of these and other results, the author concludes that the vagi and sympathetic nerves have antagonistic action on ventricular ectopic pacemakers, the former being inhibitory, the latter, augmentary.

KATZ.

Barker, N. W.: The Plasma Lipoids in Arteriosclerosis Obliterans. Ann. Int. Med. **13**: 685, 1939.

Seventy-three cases of arteriosclerosis of the legs, ranging in age from 40 to 79 years, were chosen for study in whom occlusion of the major vessels of one or both extremities had occurred and in whom x-ray evidence of classification of the arterial walls was present. A group of 200 normal individuals who lacked evidence of cardiac or vascular disease, metabolic disorders, diabetes mellitus or dermatoses served as controls. The age groups were not entirely comparable.

The total plasma lipoids and the four fractions, cholesterol, cholesterol esters, phospholipids and fatty acids, were determined on fasting bloods. An analysis of these data shows very little difference in the comparable age groups for the range, but wider variations in the mean for the arteriosclerotic group. The mean levels of cholesterol and total lipoids in the normal group were slightly lower than in the arteriosclerotic group. There was a gradual decrease in the mean value for each fraction with advancing age. One explanation for this is the fact that elderly patients frequently suffered loss of appetite and weight because of the persistent pain and loss of sleep attendant upon the presence of gangrene.

Thirty-six cases of thromboangiitis obliterans were also studied. They showed actually lower figures than either the normal or arteriosclerotic group. None exceeded 273 mg. cholesterol per 100 c.c. of blood.

The author states that in chronic occlusive arterial disease of the lower extremity where the exact nature of the lesion is indeterminate by other criteria, a plasma cholesterol value of more than 300 mg. per 100 c.c. is supportive evidence for arteriosclerosis obliterans, and that a plasma lipoid value of 200 or less is definite although not certain evidence for thromboangiitis obliterans.

Eight of the seventy-three sclerotic patients were given low fat diets; four did not show reduction in plasma lipoids, four did. In three of the four that did, pulsations of the popliteal, posterior tibial and dorsalis pedis vessels, which had been absent, were found to be almost normal. Intermittent claudication disappeared. The author notes also that of three cases of xanthoma of the skin, with marked lipemia, without diabetes mellitus, between 45 and 50, with chronic occlusive vascular disease and intermittent claudication who had been placed on a low fat diet for a year, one was relieved of his claudication and pulsations in the vessels returned.

McGovern.

Burton, A. C.: The Range and Variability of the Blood Flow in the Human Fingers and the Vasomotor Regulation of Body Temperature. Am. J. Physiol. **127**: 437, 1939.

The physical regulation of body temperature depends mainly upon the physiological control of the peripheral circulation, when the environmental temperature is below that where sweating plays a major role. The physiological control of the peripheral circulation for the regulation of the average flow to the requirements of heat elimination is mediated chiefly by the sympathetic nervous system. Evidence has been given that the activity of the sympathetic system under the influence of afferent stimuli is in a state of continual fluctuation of tone, while the activity of the sympathetic centers may be of a rhythmic and intermittent character which bears no obvious relation to any corresponding intermittence of afferent influences.

The regulation of the peripheral blood flow is concerned not only with heat elimination but also simultaneously with a supply of oxygen to meet the needs of local metabolic activity and the counteracting of changes in blood pressure and flow which might otherwise occur in tissues where constancy is of more vital importance.

In some five hundred determinations of the flow in the fingers by means of the finger plethysmograph, in seven normal subjects, the range is from 0.5 c.c. to 1.0 c.c. as a minimum up to 80 to 90 c.c. per minute per 100 c.c. of tissue for full dilatation; these experiments included the administration of constrictor and dilator drugs and the use of extremes of temperature both local and general. The minimal value found is shown to correspond with that calculated for the basal oxygen consumption of skin. The tremendous range of flow, made possible by the arteriovenous anastomoses of the fingers, represents not a metabolic need of the tissues but the mechanism for temperature regulation by elimination of body heat.

Fluctuations in the flow are rhythmic in character and simultaneous in the digits of all the extremities of the body, with an accompanying cardiac acceleration and rise of blood pressure.

The rhythm is markedly modified by the conditions of temperature regulation. The amplitude of the waves is greatest in the middle range of blood flow and of temperature, is less in dilatation, and least in constriction. The frequency of the rhythm is also modified, the faster rhythms being associated with cooler conditions and with lower average values of the flow.

Physical regulation of body temperature is accomplished, not by the setting of the peripheral blood flow to an appropriate steady level, but by the adjustment of the average of a flow which is fluctuating rhythmically between high and low values. ROTH.

Abramson, David I., Schkloven, Norman, Margolis, Meyer N., and Mirsky, I. Arthur: Influence of Massive Doses of Insulin on Peripheral Blood Flow in Man. Am. J. Physiol. **128**: 124, 1939.

A marked increase in blood flow, determined by means of the plethysmographic method, was usually observed in the hand, forearm, and leg at the height of the hypoglycemic response produced by massive doses of insulin administered to seven patients with schizophrenia. In contrast, a rapid decrease in blood flow to below the control level, especially in the hand, usually occurred with the termination of hypoglycemia by the administration of glucose either orally or intravenously. When glucose was given without the previous injection of insulin, this marked effect upon blood flow was not apparent.

During the hypoglycemic state when the blood flow to the arm was increased about 2.3 times, the forearm blood showed a very significant decrease in both oxygen and carbon dioxide arteriovenous differences. From chemical changes of the same magnitude in both brain and arm blood, previous workers have concluded that there was no significant change in cerebral blood flow during the hypoglycemic state. Therefore, the necessity for obtaining blood flow and chemical changes simultaneously was stressed by the present authors.

ROTH.

Cossio, P., and Berconsky, I.: Venous Pressure in Upper and Lower Extremities in Increased Size of the Left Auricle. Mechanism of Cyanosis in Mitral Stenosis. Rev. argent. de cardiol. **6**: 137, 1939.

Measurements of the venous pressure by the direct method were made in the antecubital vein and in the femoral vein in thirteen patients with mitral stenosis. These measurements have shown that a circulatory stasis exists in the territory of the superior vena cava due to reduction of its caliber and modification of its course as a consequence of the heart's rotation and of the change in orientation of the aorta, which occur in mitral stenosis.

The cyanosis of the face and hands and the jugular engorgement so common in mitral stenosis even without cardiac insufficiency are related to this stasis in the territory of the superior vena cava.

A new and simple model of syringe is described which makes easier the determination of the venous pressure by the direct method.

AUTHORS.

Williams, Russell D.: Electrocardiographic Changes in Acute Hemorrhagic Nephritis. Bull. Johns Hopkins Hosp. **65**: 434, 1939.

Fifteen cases of acute glomerular nephritis have been followed with serial electrocardiograms. Changes were observed in ten cases and consisted chiefly in flattening and inversion of the T waves in one or more leads, including the precordial lead. Changes were noted less frequently in the initial positive deflection in the precordial lead, and in the auriculoventricular conduction time. No correlation could be established between the occurrence of these changes and the signs of cardiac and renal insufficiency, but the series is too small to permit accurate deductions in this respect. Rabbits in which acute nephritis had been induced by the method of Masugi, failed to show comparable changes in their electrocardiographic patterns. AUTHOR.

Perschmann, G.: The Electrocardiogram Following Orthostatic Circulatory Readjustment. Ztschr. f. Kreislaufforsch. **31**: 384, 1939.

This study deals with the effect on the electrocardiogram of half-hour standing after passive placement of the patient in the erect position. Eighty-eight patients with various diseases were observed. It was found that an abbreviation of cycle length, of systolic duration, and an increase in the height of the P wave, a decrease in T wave and, in some, a depression of the S-T segment occurred. In thirteen instances a marked fall in blood pressure, with collapse, occurred. No correlation could be made between the electrocardiographic changes and the hypotension; and the S-T and T changes occurred in the absence of heart weakness or heart damage.

KATZ.

Warnecke, B.: The Electrocardiogram in Apparently Non-cardiacs Over 65 Years of Age. Ztschr. f. Kreislaufforsch. **31**: 391, 1939.

In seventy cases of apparently noncardiac elderly persons between 65 and 88 years of age, twenty-nine had normal electrocardiograms; twenty-five had evidences of mild conduction disturbances; sixteen had changes in the S-T segment and T complex of the coronary insufficiency variety, or intraventricular block.

KATZ.

Videla, Jorge Gonzalez: Deep Q Wave in Lead III of the Electrocardiogram. Its Importance in Varying Degrees of Deep Inspirations. Rev. argent. de cardiol. **6**: 146, 1939.

A series of thirty electrocardiograms with large Q_3 according to Pardee's criteria were analyzed, and the effect which deep inspiration has on the size of Q_3 and R_3 was studied. The conclusion is reached that when its reduction in size is less than 50 per cent of that of the R_3 wave, the large Q_3 is due to myocardial damage of organic or ischemic origin. On the contrary when the percentage reduction is high, 75 per cent or more, the large Q_3 is due to a mechanical cause (elevation of the diaphragm, etc.) and has no pathologic significance.

AUTHOR.

Mainzer, F., and Krause, M.: Changes of the Electrocardiogram Brought About by Fear. Cardiologia. **3**: 286, 1939.

Fear (of the impending operation) may induce considerable changes of the electrocardiogram (taken on the operating table before the onset of narcosis).

Under these circumstances the electrocardiographic curve can gain a pathologic aspect even in persons, healthy, with regard to their hearts. In two persons suffering from cardiac disturbances the changes were particularly marked.

The changes can be classified in two categories:

1. P and T increase in amplitude and become pointed.

2. The size of the ventricular complex diminishes, the T deflection becomes negative, S-T descends below the isoelectric level and becomes deformed.

The former changes may be due to a sympathetic stimulus of the heart contraction, the second group to coronary constriction, possibly caused by vagal stimulation.

It is shown that some electrocardiograms of neurasthenic persons who have healthy hearts can assume an analogous character, probably through pure fear. These are "fear-electrocardiograms," which must not be connected with organic cardiac disturbances.

AUTHORS.

Rosenbaum, Francis F., and Levine, Samuel A.: Auricular Standstill. Its Occurrence and Significance. Am. J. Med. Sc. **198**: 774, 1939.

This series of eight cases of auricular standstill (with four other probable cases) confirms the belief that digitalis or quinidine intoxication is the most common cause of auricular standstill. When there is electrocardiographic evidence of its presence, the nature and dosages of the drugs being given the patient should be investigated and adjusted. This group of cases further indicates that the disorder tends to occur more commonly in older patients who are in congestive failure from serious heart disease. Particularly in view of Case 1, whose pulse and respirations were seen to cease for a short time and in whom auricular standstill was known to exist both before and immediately after this event, we believe it is well to re-emphasize the fact, pointed out by Wolff and White, that the mechanism responsible for this cardiac disorder may be closely related to some instances of sudden death during digitalis or quinidine therapy. Finally, it would appear from these cases that auricular standstill resulting from quinidine tends to be far more transient than that due to digitalis.

AUTHORS.

Hecht, A.: Alterations of the Heart Chambers in Hypertension and Valvular Defects. Arch. f. Kreislaufforsch. **5**: 73, 1939.

Studies were made of postmortem fixed heart specimens. In pure left-sided strain, the sulcus longitudinalis anterior is shifted to the right. The right ventricle is pushed dorsad and upward and to the right. The outflow tract of the left ventricle is elongated, and only the left ventricle wall is thickened.

In pure right-sided strain, the left ventricle is normal; the right ventricle is widened, the apex may be formed by the right ventricle.

In combined right and left strain, the dislocation of the anterior longitudinal sulcus is as in pure left ventricular strain, otherwise there is a combination of changes of the individual ventricles. In an enlarged athlete's heart no alterations in contour of the heart were found but merely a larger size.

KATZ.

Bunim, Joseph J., and McEwen, Currier: The Antistreptolysin Titer in Rheumatic Fever, Arthritis and Other Diseases. J. Clin. Investigation **19**: 75, 1940.

The results of 1,539 determinations of the antistreptolysin titers of the sera of 817 patients are here reported.

In normal individuals we have found the median titer to be 25 units and the normal maximum titer to be 100 units per c.c.

Eighty per cent of patients with scarlet fever showed a rise in antistreptolysin titer during the course of the disease, but in only 48 per cent did it rise above 100 units in the three- to four-week period of observation.

The majority of all patients with active rheumatic fever showed a high antistreptolysin titer. The incidence of elevated titers bore no relation to the various clinical manifestations of the rheumatic infection. Those patients whose illness was preceded by an upper respiratory infection sufficiently severe to be remembered, showed this immunologic response more commonly than those without a history of preceding upper respiratory infection. Patients with inactive rheumatic heart disease usually had normal titers.

The majority of patients with chorea showed an increased titer regardless of whether or not the condition was associated with heart disease or polyarthritis. Age, severity of illness, and fever therapy did not seem to influence the antibody titer.

Patients with rheumatoid arthritis, as a rule, did not show an abnormal antistreptolysin titer. This is in sharp contrast to the high incidence of raised hemolytic streptococcus agglutinin titers observed in these patients even when the identical strain was used as an antigen to measure both antibodies.

Patients with other types of arthritis similarly failed to show an elevated antistreptolysin titer in a significant percentage of cases.

Because three-quarters of the patients with rheumatic polyarthritis showed an abnormally high titer and those with other forms of joint diseases did not, the test was found helpful in diagnosis.

Patients with erythema nodosum of hemolytic streptococcal origin and patients with acute pericarditis of rheumatic type had, as a rule, an abnormal titer. When, however, these conditions were of a tuberculous origin, the titer was within normal limits. Here again the serologic determination may be of diagnostic value. Further studies are needed to corroborate this impression since the number of cases here reported is small.

Several patients with *lupus erythematosus disseminatus* and periarteritis nodosa had a normal antistreptolysin titer.

In no disease have we found a correlation between the antistreptolysin titer and the severity of the illness; hence the titer is of doubtful prognostic significance.

Finally, it must be borne in mind that an elevated antistreptolysin titer may be found in a patient suffering with a disease not related to, but merely preceded by, a hemolytic streptococcus infection. To reason that the elevated titer indicates that the presenting disease is of hemolytic streptococcal origin may lead to an erroneous diagnosis.

AUTHORS.

Stead, Eugene J., Jr., and Kunkel, Paul: Nature of Peripheral Resistance in Arterial Hypertension. J. Clin. Investigation **19**: 25, 1940.

The increased peripheral resistance present in arterial hypertension cannot be reduced to the normal level in the skin of the hand and the foot, the muscles of the forearm, or in the brain by powerful vasodilating stimuli.

The blood flow in the hand and foot at 43° C. and in the muscles of the forearm after exercise shows no significant difference in normal and in hypertensive subjects.

In hypertensive subjects cerebral anoxia does not reduce the peripheral resistance in the vessels of the brain to normal levels. Therefore, in postural experiments after the administration of sodium nitrite, subjects with arterial hypertension develop syncope with a much higher arterial pressure than do normal subjects.

The finding of a uniform degree of elevation of the peripheral resistance throughout the body is strong evidence against the neurogenic origin of the usual types of clinical hypertension because the nervous vasomotor control is different in each of the tissues investigated.

In one subject with arterial hypertension, a marked fall in arterial pressure after malaria produced no change in the blood flow in the foot at 43° C., indicating that no structural changes had taken place in the vessels. In a second subject the blood flow in the foot at 43° C. was decreased when the arterial pressure fell, indicating that permanent vascular damage had occurred. The arterial hypertension in both of these subjects originally resulted from active vasoconstriction. In one structural changes had later developed.

Sensory stimuli, such as pinch, noise, and deep breath, produce vasoconstriction of similar degree in both normal and hypertensive subjects. When the arterial pressure is greatly lowered following malaria, these vasoconstrictor responses remain unchanged.

In arterial hypertension the peripheral resistance is uniformly raised throughout the area of the greater circulation, and it is not increased in the splanchnic area to any greater extent than in other tissues.

AUTHORS.

Baylin, George J.: Collateral Circulation Following an Obstruction of the Abdominal Aorta. Anat. Rec. **75:** 405, 1939.

The collateral circulation is described in a patient, male, aged 34 years, who had a clot with calcification in the abdominal aorta just distal to the orifices of the renal arteries. The most important collateral channel was the colic anastomosis. The superior mesenteric artery and its middle colic branch were almost as large as the aorta, and joined directly with the equally enlarged left colic branch of the inferior mesenteric artery. Other channels of collateral circulation were the somewhat enlarged and tortuous internal mammaries which joined the inferior epigastric arteries on either side. The last three pairs of intercostal arteries were enlarged and tortuous and made numerous connections with other vessels. These connections were important, but subordinate to the anastomosis between the two mesenteries.

NAIDE.

Fitz, Reginald, Parks, Harry, and Branch, Charles F.: Periarteritis Nodosa. Arch. Int. Med. **64:** 1133, 1939.

A case of periarteritis is reported in a patient, female, aged 37 years, who had symptoms of the disease for eleven years before death. The patient was studied during twenty months of almost continuous hospitalization so that a fairly complete account of the evolution of the disease in this case was developed. Complete necropsy findings are reported.

NAIDE.

McLaughlin, C. W., Jr., and Pompa, A. M.: Intermittent Obstruction of the Subclavian Vein. J. A. M. A. **113:** 1960, 1939.

The report concerns intermittent occlusion of the subclavian vein in a 24-year-old farmer. Swelling and cyanosis of the entire right upper extremity followed exertion and subsided with rest over a period of two years. Cervical pain accompanied these symptoms. Eight years prior to present illness, he sustained a fracture of both bones of the right forearm which healed without deformity.

No sensory disturbance or loss of strength was noted. X-ray photographs to be taken after collodial thorium dioxide was injected into the median cubital vein and into the axillary vein showed clearly an obstruction or narrowing of the vein as it crossed the first rib.

At operation the narrowing was confirmed and the scalenus anticus muscle was sectioned, allowing the rib to slip downward, and relieving the obstruction.

Ten days following operation, exercise failed to produce edema or cyanosis; and both arms were the same diameter. Venagran showed the vein to be normal in size and position.

MCGOVERN.

Stewart, Harold J., and Watson, Robert F.: The Circulation in Athletes. J. Clin. Investigation **19:** 35, 1940.

Measurements of the arteriovenous oxygen difference, oxygen consumption, minute volume output, stroke volume, vital capacity, cardiac size, circulation time and

venous pressure, arterial pressure and heart rate, were made of fourteen college athletes and also of eleven healthy, young, adult males who were living a sedentary life and who served as controls. These objective measurements were carried out under basal conditions.

With one exception, there was no significant difference between those made on college athletes and those derived from the control group. The stroke volume of the athletes was slightly larger. This difference appears to be related to body size, since the stroke volume per kilogram of body weight and the cardiac index for the two groups are approximately the same.

AUTHORS.

Strasberg, Alex: Peripheral Vascular Complications in Prostatic Surgery. Canad. M. A. J. **41**: 377, 1939.

The title of the article is a little confusing. Three reported cases appear to have died from embolic phenomena to the lungs. There is nothing new except the mention of heparin to prevent thrombosis. Thrombosis-embolism is a fatal complication in 2 to 7 per cent of prostatic operations.

MCGOVERN.

Holland, Dorothy F.: The Disabling Diseases of Childhood. Their Characteristics and Medical Care as Observed in 500,000 Children in Eighty-Three Cities Canvassed in the National Health Survey of 1935-1936. Am. J. Dis. Child. **58**: 1157, 1939.

This report is a public health statistical analysis of the usual disabling diseases occurring during childhood. It is important because of the method of study, as well as the observations which are made. These are related particularly to the importance of ordinary diseases. It is interesting to note that rheumatic fever and heart disease in children occupy a low portion in the frequency rate as compared with diseases of the respiratory system and other communicable conditions. The frequency rate is 1.2 as compared with 0.5 for tuberculosis, and 73.9 for diseases of the respiratory system. This figure coincides with prevailing impressions as to the frequency of rheumatic heart disease obtained from other surveys.

MCCULLOCH.

Kitchen, I. D.: The Treatment of Seven Cases and Complication of Varicose Veins in the Legs. Canad. M. A. J. **41**: 374, 1939.

This article describes the technique for ligation and retrograde injection of varicose veins of the leg and the two tests commonly used for determining the competency of the valves of the communicating veins. The author states that the commonest sites for a venous blowout are just above and below the knee and in midthigh. The presence of pelvic tumor, active inflammation in the groin, and ulcers are contraindications for surgical treatment.

Where there has been ulceration and scar formation, a Kondalion procedure is done, which is followed by a skin grafting procedure that incapacitates the patient for a period of eight weeks.

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THE American Heart Association, sponsor of the first International Health Broadcast, stands alone as the national organization devoted to educational work relating to diseases of the heart. Its Board of Directors is composed of twenty-five physicians representing every portion of the country.

The Section for the Study of the Peripheral Circulation was organized in 1935 for the purpose of stimulating interest in investigation of all types of diseases of the blood and lymph vessels and of problems concerning circulation of blood and lymph. Any physician or investigator in good standing may become a member of the section after election to the American Heart Association and payment of dues to that organization.

To coordinate and distribute pertinent information, a central office is maintained, and from it issues an ever widening stream of books, pamphlets, charts, posters, films, and slides. These activities all concern the recognition, prevention or treatment of the leading cause of death in the United States, diseases of the heart. The AMERICAN HEART JOURNAL is under the editorial supervision of the Association.

The income from membership and donations provides the sole support of the Association. Lack of adequate funds seriously hampers more widespread educational and research work imperative at this time. Great progress has been made, but much remains to be done.

Annual membership is $5.00 a year and journal membership at $10.00 includes a year's subscription (January-December) to the AMERICAN HEART JOURNAL and annual membership in this Association. A cordial invitation to join in this crusade is extended to you.

The American Heart Association solicits your support to the end that it may continue more effectively the campaign to which it has devoted all its energy.

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